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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.

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THE PREPARATION AND SOME FEATURES OF THORIUM SULFIDES

G. V. Samsonov and N. M. Popova

The sulfides of thorium form an interesting group of compounds, and the study of their properties leads not only to their use in certain branches of technology but also to definite conclusions on the nature of the chemical bond in the sulfides of transition metals. The reaction of the Th atom, which has an incomplete inner 5f - electron level (1 electron out of 14), with sulfur, whose atoms give up the outer s - and p - electrons comparatively easily (the first ionization potential of sulfur equals 10.31 ev), might be expected to lead to the setting up of an electronic interaction in the Th and S atoms, which would result in the formation of a metallic bond and give them their characteristic metallic properties, in a similar fashion to that which obtains in the carbides, borides, nitrides and in particular the silicides of the transition metals, with this one difference, that covalent bonds between the Si atoms play a definite part in the silicide structures, whereas in the sulfides the role of the covalent S-S bonds is relatively slight.

Similar conclusions may be reached by applying to the thorium sulfides the criterion 1/Nn, established by us earlier [1], where N is the principal quantum number and n the number of electrons in the incomplete sublevel. For Th this factor equals 0.2, while for Ti, for example, it is only 0.167 and for Zr, 0.125 etc., which leads to a fairly real probability that the outer electrons of the sulfur enter the f-level of the thorium. The radius of the sulfur atom, however, is large by comparison with the radii of the atoms of B, C, and N, which excludes the possibility of compound formation involving interstitial phases — the compounds should consist of substitutional phases. This should considerably reduce the " interlocking " of the planes of the metallic lattice and as a result should bring about a decrease in hardness and brittleness and an increase in the plasticity of the thorium sulfides, in spite of the considerable strength of the bond between the atoms of Th and S. It must also be assumed that solubility of S in Th, i.e., the extent of a metallic phase, is very insignificant.

The existence of four sulfides of thorium is indicated in the literature: ThS, Th_4S_7 (or Th_7S_{12}), Th_2S_3 and ThS_2. The composition diagram for Th – S has not been studied, so that the question of whether one or other of the thorium compounds is actually present can only be judged on the basis of preparative works, of which the most significant is [2]. A survey of the properties of thorium sulfides is given in the works [2-10], and some data from these are given in Table 1.

The following somewhat fragmentary data are given in the literature on the preparation of thorium sulfides.

The thermal dissociation of higher sulfides [2]. In the dissociation, a reactor with controlled pressure is used and by altering the pressure it is possible to vary the Th:S ratio in the products obtained. Using this method, for example, the sulfide Th_4S_7 is obtained by the dissociation of ThS_2 or of thorium polysulfide ThS_x.

It is pointed out in the patent literature [11] that the decomposition of ThS_2 by heating for 3 hours at 1900-2000° and 10^{-5} mm pressure yields sulfides with S:Th ratio = 1.75.

Heating higher sulfides with thorium or thorium hydride. According to the data in [11], ThS may be obtained by heating a stoichiometric mixture of ThS_2 and Th at 1850-1900° below atmospheric pressure for 30 minutes. When the briquet is ground to powder and heated again under the same conditions the reaction goes to completion and the product is obtained as one phase.

Heating Th, thorium carbide or ThH_4 with sulfur or hydrogen sulfide. In the work described in [2], the preparation of ThS_2 was carried out by heating a mixture of Th (in the form of turnings) and sulfur under

Certain Properties of Thorium Sulfides

Property	Sulfides			
	ThS	Th_3S_7 or Th_7S_{12}	ThS_2	Th_2S_3
Color	Grey with metallic luster [5]	Red	Yellow-brown [6] to black [7]	Brown
Crystal structure	NaCl [2]	Hexagonal [10]	Rhombic [5]	Rhombic [5]
Lattice parameters (A)	4.674 [2] 5.671 [10]	$a = 11.041$ $c = 3.983$ [10]	$a = 4.259$ $b = 7.249$ [10] $c = 8.600$	$a = 10.97$ $b = 10.83$ [10] $c = 3.95$
Density (g/cm^3)	8.91 [2] 9.56 [5]	6.91 [2]	7.30 [2] 7.36 [5]	9.57—9.69 [2]
Melting point (°C)	> 2500 [8] > 2200 [5]	~ 2300 [8] 1770 ± 30 [5]	2203 [8] 1905 [5]	~2300 [8] 1900—2000 [5]
Heat of formation (kcal/mole)	120 ± 50 [8]	665 ± 35 [8]	170 ± 20 [8]	306 [8]
Vapor pressure (mm Hg)	10^{-3} at 2200° [9]	—	43 at 651°) 163 at 713°) [2] 382 at 754°)	
Magnetic properties	Diamagnetic	—	—	Diamagnetic

pressure for 18 hours at 600°, 100 hours at 780 - 800°, after which it was cooled over a period of several hours (6 - 8 hours). In the same way thorium polysulfides with a sulfur content up to an apparent formula ThS_{10} have been prepared. The reference book [6] indicates the possibility of preparing the sulfides ThS_2 and Th_3S_7 by the direct union of Th and S at 600 - 800°. Thorium sulfides are also obtained by heating stoichiometric quantities of ThH_4 and H_2S at 400 - 500° below atmospheric pressure or by heating ThS_2 with partly decomposed hydride and with H_2S at 500 - 600° [12]. As a variation of the method of synthesis, the preparation of thorium sulfides by heating ThO_2 in the presence of carbon in a stream of H_2S [9] or by heating ThC_2 with sulfur [13] has been suggested. References to the older descriptions of these methods are given in the monograph [5].

Heating thorium chlorides with H_2S. Duboin [14] and Kruss [15] have prepared thorium sulfides by the action of H_2S on a mixture of the chlorides of thorium and sodium; the products obtained in this way were contaminated, according to their data, by oxysulfides. The same method is recommended in a patent [9], where the use of sulfur in place of hydrogen sulfide is suggested as an alternative.

There are also descriptions of methods of preparing thorium sulfides by the action of carbon disulfide and hydrogen on thorium dioxide, and also by the action of carbon disulfide on a mixture of thorium dioxide and carbon [5].

EXPERIMENTAL *

The aim of our work was to render more precise the method for preparing sulfides of thorium by the direct union of thorium and sulfur.

The starting materials were thorium powder with a Th content of 99.8 % and carefully purified flowers of sulfur. In the study of the preparation conditions for the sulfides, four mixtures were taken corresponding to the conditional formula ThS_x, where x = 1.00, 1.25, 1.50, 2.00. The samples were placed in porcelain boats set up in a tube furnace with a porcelain tube through which an uninterrupted stream of hydrogen sulfide was passed. The boats were set up in the furnace at the temperatures given. The first series of experiments was carried out at temperatures from 400 - 850° at intervals of 50 - 100°, each experiment lasting for 30 minutes. In part of the experiments the products obtained were cooled in air, and in part they were cooled in a stream of H_2S.

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* L.G. Kurova took part in the experimental part of the work.

The results obtained in this way are given in Figure 1, from which it is seen that with the products cooled in air the sulfur content rises with temperature, reaching a maximum value at 600°. When the temperature is raised further the sulfur content in the products is somewhat lowered. At the same time all the products contain oxygen (the sum $Th + S_{total} = 92 - 98\%$), which either is not removed during the heating process or enters the products during the cooling process.

In none of the products does the sulfur content reach that required by the formula ThS_2, but varies between the limits $ThS_{0.38}$ and $ThS_{1.62}$.

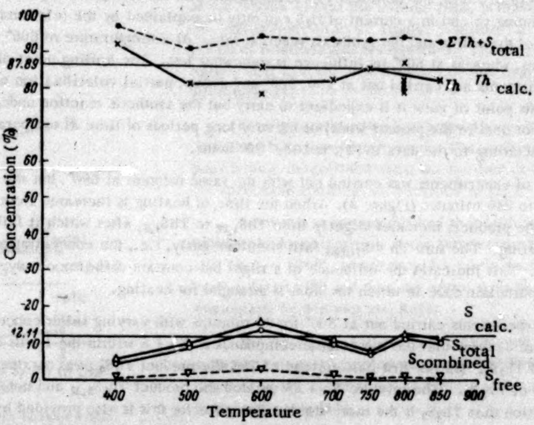

Fig. 1. The relationship between the chemical composition of thorium sulfide and temperature (maintained for 30 minutes).

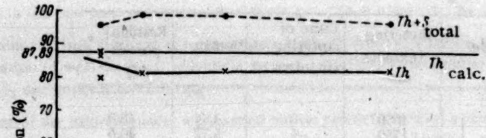

Fig. 2. The relationship between the chemical composition of thorium sulfide and the time of heating (temperature 600°).

When the reaction products are cooled in a stream of hydrogen sulfide, the sulfur content is raised sharply, while the sum of the concentrations Th + S_{total} reaches 100 %, particularly in the experiments carried out at 600°. The composition of the products obtained in this way, assuming that no free thorium is present (which is confirmed by x-ray analysis), may be expressed by the formula $ThS_{\sim 1.5}$ i.e. Th_2S_3. It should be noted that in spite of the identical conditions under which the experiments were carried out, the variation in the composition of the products is considerable, which suggests the effect of kinetic factors, such as, for example, the thickness of the layer of the charge, the uniformity of the charge in the boat, the degree of mixing of the components, etc.

Since the greater part of the total sulfur in the products is in the combined state and the free sulfur concentration is small (0.3 0.5%), the deficiency of sulfur relative to the formula ThS_2 in the experiments carried out from beginning to end in a current of H_2S can only be explained by the relationship between the rate of volatilization of the sulfur and the synthesis reaction rate. At a temperature of 600° the first process evidently predominates, whereas at 800° its influence is somewhat less. The boiling point of sulfur is 444.6°, so that when the experiments are carried out at 400, 500° and above, partial volatilization of the sulfur is unavoidable. From this point of view it is expedient to carry out the synthesis reaction under increased pressures (which was not done in the present work) or for very long periods of time at temperatures below 400°. The time required, according to the data in [2], is 100 - 200 hours.

The next series of experiments was carried out with the same mixture at 600°, but the time of heating was changed from 30 to 240 minutes (Figure 2). When the time of heating is increased from 30 to 60 minutes, the sulfur content in the products increases slightly from $ThS_{1.22}$ to $ThS_{1.5}$, after which it falls regularly with increasing time of heating. The sum Th + S_{total} falls simultaneously, i.e., the concentration of oxygen in the samples increases. This indicates the influence of a slight but constant diffusion of oxygen into the furnace, probably through the porcelain tube in which the boat is arranged for heating.

The results of experiments carried out at 800° for 30 minutes with varying sulfur concentration in the starting mixture (Figure 3) show that the most stable compounds of Th + S within the limits of composition indicated are ThS and Th_2S_3. (In the first case instead of ThS the product $ThS_{0.9}$ was obtained, in the second case – $Th_2S_{3.2}$ instead of Th_2S_3. The mixture Th + 2S yielded the product $Th_2S_{3.12}$ and not ThS, which leads to the indirect conclusion that Th_2S_3 is the more stable. Evidence for this is also provided by the results of experiments with the mixture Th + 2S carried out with varying temperature and sulfidization times. Many of the specimens prepared were subjected to x-ray analysis with copper K α-radiation and exposures of 6-8 hours.

TABLE 2

Sintering of ThS and Th_2S_3 with Hot Compression at 350 kg/cm^2 Pressure

Sulfide	Sintering temperature	Time of sintering (in minutes)	Density	Residual porosity (%)
Th_2S_3	1650°	8	4.94	48.8
	1750	5	5.72	40.6
	1960	8	7.66	20.3
	2100	Melted	—	—
ThS	1810	5	5.82	34.8
	2030	8	8.53	4.2
	2160	8	7.47	16.1
	2230	Melted	—	—

The specimens of composition $ThS_{1.03}$ with Th + S content 95.49% (remainder oxygen) were found to have the NaCl type lattice, as in pure ThS, but with a greater period than ThS, namely 5.615 A. The product is evidently thorium oxysulfide with composition ~ $Th_{1.3}S_{1.3}O$. (The existence of an oxysulfide ThOS is indicated in the literature [5]. The ThS specimens containing no oxygen were found to have periods of 4.66-4.69 A, i.e., values close to those given in the literature [2] for the period of pure ThS.

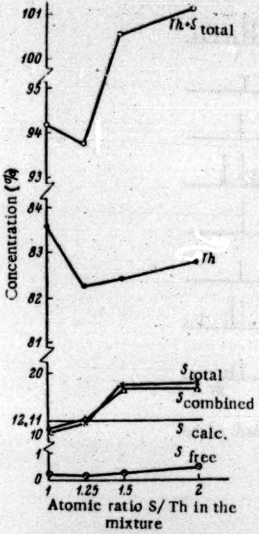

Fig. 3. Relationship between the chemical composition of thorium sulfide and the concentration of sulfur in the starting mixture.

X-ray analysis of the sulfides ThS_x, where x= 1.22-1.59, shows (Figure 4) that the sulfide Th_2S_3 is homogeneous, at least in the region from 55 to 62 atomic % sulfur, i.e., it is a typical compound of intermediate composition. The line diagram of Th_2S_3 agrees well with the line diagram of this compound given in the literature [2].

Finally, certain physical properties of the thorium sulfides ThS and Th_2S_3 were determined. The melting points of these compounds were determined using the method of direct observation of the specimens melting, as described in [16].

From this it was established that both sulfides melt without noticeable decomposition at the temperatures: ThS ~ 2400-2450° and Th_2S_3 ~ 2300°, which provides fairly good confirmation of the earlier data in [8] and does not agree with the data given in the monograph by Seaborg and Katz.

For the study of the microstructure and microhardness of thorium sulfides, compact samples were prepared from them by sintering the powders by hot compression in a press whose construction is described in the reference [17].

The results obtained in this way are given in Table 2.

From these data, and also from observations during the sintering, it can be seen that the sulfides react with the graphite of the compression mold at temperatures below those required to convert the specimen to the compact condition; in this respect ThS is evidently the more stable.

The specimens of Th_2S_3 sintered at temperatures 1960-2000° have a structure consisting of two phases, showing the separation of well-defined polyhedra against a background of mother solution (Figure 5), which indicates that Th_2S_3 decomposes on sintering.

Measurement of the microhardness was carried out on powder particles embedded in polymerized bakelite, and also on microsections of the sintered samples and of the same samples, when these had been carefully annealed (Table 3).

Attention is drawn to the considerable internal stresses which arise during sintering by hot compression and which are difficult to eliminate in the subsequent annealing, and also to the dependence of the microhardness numbers on the load on the diamond pyramid of the PMT-3 apparatus. This underlines yet once more the considerable plasticity of the thorium sulfides. The properties of the compounds of transition metals with a large deficiency of electrons in the d- or f-level (Ti, Zr, Hf, Th, V) change regularly along the series: silicides > phosphides> sulfides, as a result of the common bond type between the atoms of metal and metalloid and the identical bond type between the atoms of the metalloid, whose stability decreases from the silicides [18, 19] to the phosphides [20] and then to the sulfides. The sulfides of transition metals with a slight deficiency of electrons in the inner levels (Nb, Ta, Cr, Mo, W, U) approach ionic compounds in the bond type between the atoms of the metal and metalloid. In this respect it is interesting to make a study of these compounds and also of the chlorides and oxides of thorium, titanium etc., in which indications should be found of the presence of metallic bonds between the atoms of the metal and chlorine or oxygen.

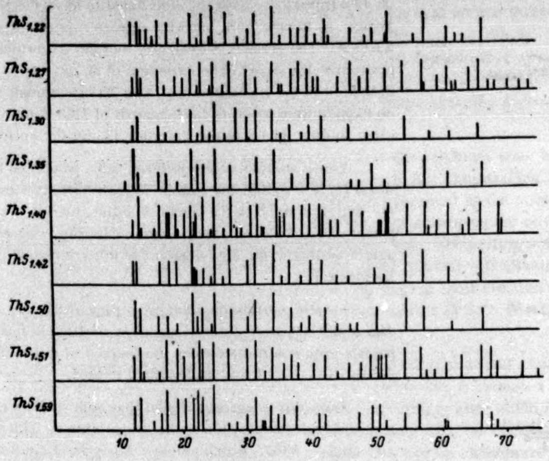

Fig. 4. Line diagrams from the X-ray diagrams of the specimens of the sulfide Th_2S_3 in its homogeneous region.

TABLE 3

Microhardness of Sulfides of Thorium

Sulfide	Microhardness (kg/mm²)		
	Powder particles	Sintered specimen	Sintered specimen after annealing
ThS	143.4±29 (5 g)	800±81.6 (30 g)	363±39.8 (20 g)
Th_2S_3* . .	171.1±29.91 (5 g)	539±45 (30 g)	227±28 (5g)

---

* For the predominant phase in the chemical compound in the Th_2S_3 specimens.

Fig. 5. Microsection of a sintered specimen of Th_2S_3 (× 596).

SUMMARY

1. The conditions for preparing thorium sulfides by the direct combination of thorium and sulfur have been made more precise.

2. It has been shown that the most stable sulfide phases of the Th-S system are ThS and Th_2S_3, while it has been established that in the formation of ThS, oxygen may enter the lattice together with the sulfur, thus bringing about an increase in the period of the lattice. It has also been observed that the compound Th_2S_3 is a phase of intermediate composition, homogeneous at least between $ThS_{1.22}$ to $ThS_{1.59}$.

3. The melting points of ThS and Th_2S_3 have been made more precise, their microhardness numbers have been determined, and a connection has been shown between the properties of the thorium sulfides and those of other analogous compounds of the transition metals with metalloids.

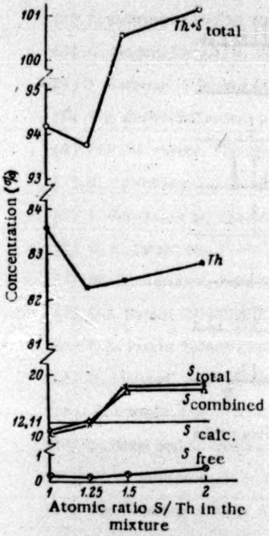

Fig. 3. Relationship between the chemical composition of thorium sulfide and the concentration of sulfur in the starting mixture.

The specimens of composition $ThS_{1.03}$ with Th + S content 95.49% (remainder oxygen) were found to have the NaCl type lattice, as in pure ThS, but with a greater period than ThS, namely 5.615 A. The product is evidently thorium oxysulfide with composition ~ $Th_{1.5}S_{1.5}O$. (The existence of an oxysulfide ThOS is indicated in the literature [5]., The ThS specimens containing no oxygen were found to have periods of 4.66-4.69 A, i.e., values close to those given in the literature [2] for the period of pure ThS.

X-ray analysis of the sulfides ThS_x, where x= 1.22-1.59, shows (Figure 4) that the sulfide Th_2S_3 is homogeneous, at least in the region from 55 to 62 atomic % sulfur, i.e., it is a typical compound of intermediate composition. The line diagram of Th_2S_3 agrees well with the line diagram of this compound given in the literature [2].

Finally, certain physical properties of the thorium sulfides ThS and Th_2S_3 were determined. The melting points of these compounds were determined using the method of direct observation of the specimens melting, as described in [16].

From this it was established that both sulfides melt without noticeable decomposition at the temperatures: ThS ~ 2400-2450° and Th_2S_3 ~ 2300°, which provides fairly good confirmation of the earlier data in [8] and does not agree with the data given in the monograph by Seaborg and Katz.

For the study of the microstructure and microhardness of thorium sulfides, compact samples were prepared from them by sintering the powders by hot compression in a press whose construction is described in the reference [17].

The results obtained in this way are given in Table 2.

From these data, and also from observations during the sintering, it can be seen that the sulfides react with the graphite of the compression mold at temperatures below those required to convert the specimen to the compact condition; in this respect ThS is evidently the more stable.

The specimens of Th_2S_3 sintered at temperatures 1960-2000° have a structure consisting of two phases, showing the separation of well-defined polyhedra against a background of mother solution (Figure 5), which indicates that Th_2S_3 decomposes on sintering.

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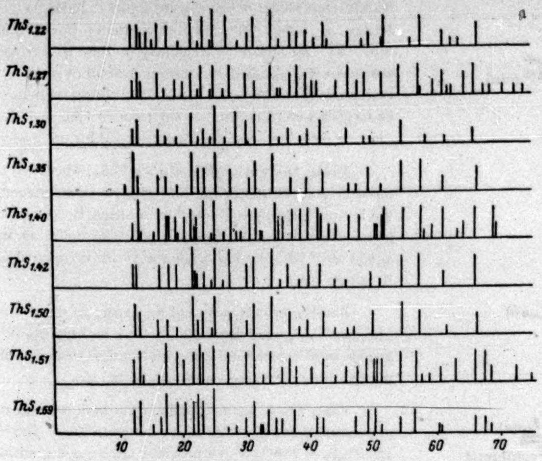

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LITERATURE CITED

[1] G. V. Samsonov, Proc. Acad. Sci. USSR 93, 689 (1953).

[2] E. E. Strotzer and M. Zumbusch, Z. anorg. u. allgem. Chem. 247, 415(1941).

[3] G. Jaeger, Metall. 9, 358 (1955).

[4] E. Eastman, L. Brewer, A. Bromley, R. Gilles and N. Longfreen, J. Am. Chem. Soc. 34, 128(1951).

[5] The Actinides,* edited by G. Seaborg and J. Katz (Foreign Lit. Press, 1955), p. 75.

[6] M.P. Slavinsky, The Physicochemical Properties of the Elements (Metallurgical Press, 1952).**

[7] B. V. Nekrasov, A General Chemistry Course (State Chem. Press, 1952).**

[8] L. Brewer, et al., Thermodynamic Data of Miscellanous Materials (New York, 1948).

[9] U. S. Patent No. 791466 (1949).

[10] W. Zachariasen, Acta Cryst. 2, 189 (1949).

[11] U.S. Patent 791469 (1950).

[12] U.S. Patent 791468 (1950).

[13] H. Moissan, A. Etard, Compt. rend. 122, 573 (1896); Ann. chim. et phys. (7) 12, 497 (1897).

[14] A. Duboin, Compt. rend. 146, 815 (1908).

[15] G. Kruss and C. Volck, Z. anorg. Chem. 5, 75 (1894).

[16] G. V. Samsonov, E. V. Petrash, Metallography and the Treatment of Metals (1955), 1, 19.**

[17] The Working of Solid Alloy Tailings.** (TsITEIN Library, 1943), No. 1.

[18] H. Wallbaum, Z. Metallkunde 33, 378 (1941).

[19] G. B. Boky, Introduction to Crystal Chemistry (Moscow State University Press, 1954), p. 327.**

[20] N. Schonberg, Acta Chem. Scand. 8, 226 (1951).

Received February 16, 1956

The Moscow Institute of Gold and Nonferrous Metals

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* Russian translation.

** In Russian.

[1] G. V. Samsonov, Zhur. neorg. Khim. [illegible] (1956).

[2] E. E. Samsonov and M. Zeitsman, [illegible]

[3] [illegible] (1959).

[4] C. Agte, [illegible]

[5] The Metallurgy [illegible]

[6] M.P. Slavinsky, The Physico-chemical Properties of the Elements [illegible]

[7] G. V. Samsonov, [illegible]

[8] R. Kieffer, et al. [illegible]

[9] U.S. Patent No. [illegible]

[10] M. Zeitsman, [illegible]

[11] U.S. Patent [illegible]

[12] U.S. Patent [illegible]

[13] [illegible]

[14] A. Dubois, [illegible]

[15] [illegible]

[16] G. V. Samsonov, [illegible]

[17] The working of Solid Alloy [illegible]

[18] [illegible]

[19] G. V. Samsonov, [illegible]

[20] [illegible]

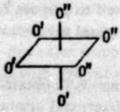
- * Russian translation.
- ** In Russian.

THE PREPARATION OF BARIUM CIS–BOROTUNGSTATE

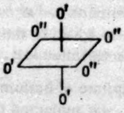
E. A. Nikitina and O. N. Sokolova

Borotungstic acid with general formula $H_9[B(W_2O_7)_6] \cdot H_2O$ is known in two forms possessing different properties; corresponding to each of these forms is a series of salts of identical composition but with different physico-chemical properties. As a result of this it is difficult to say that the borotungstic acids are different hydrated forms of one and the same heteropolyacid. There is much more justification for considering them as two-layer isomeric cis- and trans-borotungstic acids in which the central boron ion is surrounded octahedrally (according to Pfeiffer) by non-equivalent oxygen ions:

$H_9[BO_6(WO_3)_{12}] \cdot xH_2O$



Cis-form



Trans-form

The borotungstates (hereafter referred to as the B.T.) are the most difficult of the heteropolycompounds of the saturated series to prepare, and their analysis is also extremely complicated. It is therefore not surprising that in the earlier literature [1] formulas are given for one and the same compound with the different $B:WO_3$ ratios = 1:9, 1:12 and 1:14.

Recently, Souchay [2] has indicated the existence of B.T. salts of the 11 series, but these data require further experimental confirmation.

EXPERIMENTAL

a) The synthesis of sodium borotungstate. Sodium borotungstate was used as the starting material for the synthesis of the remaining B.T.'s.

According to the literature data, the process of complex formation between the BO^{3-} and WO^{4-} ions is a reaction taking some time for completion, is not always reproducible, and requires a quantity of H_3BO_3 100 times in excess of that calculated according to the equation

$$2H_3BO_3 + 24Na_2WO_4 + 38\ HCl = 2Na_5H_4[B(W_2O_7)_6] + 38NaCl + 18H_2O.$$

Repeated recrystallization is necessary to obtain the sodium B.T. in the pure state, and this introduces a number of difficulties.

The experiments carried out by us have shown that the formation of the complex goes to completion even with stoichiometric amounts of $Na_2WO_4 + H_3BO_3$, which considerably simplifies the main process – the formation of the anion $[B(W_2O_7)_6]^{IX}$:

The method worked out by us for the preparation of sodium B.T. was as follows: 100 g $Na_2WO_4 \cdot 2H_2O$ was dissolved in 300 ml boiling water; 1.55 g H_3BO_3 was dissolved separately in 25 ml water heated similarly to boiling point, and the two solutions obtained were poured together. Concentrated hydrochloric acid (70–75 ml) was slowly added dropwise by hand to the boiling solution of the mixed components, with continued heating and vigorous stirring, to an acid reaction with Congo red (ph approximately 3.5). The solution obtained was heated for 18 hours, keeping the volume constant (by adding water). At the end of this time the sodium B.T. solution was filtered from the slight precipitate. The volume of solution after filtration was approximately 300 ml (d^{20}1.30–1.32). Such a solution contains approximately 75 g sodium B.T.

b) The synthesis of barium borotungstate. Two barium salts of borotungstic acid are known from the literature: barium cis-B.T. – the water-soluble salt – and barium trans-B.T. – a compound soluble with difficulty.

The method for preparing barium B.T. described in the literature involves the action of a large excess of barium chloride on a solution of sodium B.T. The barium salt of the trans-form separates as a precipitate which is increased on cooling and is easily separated from the solution. The precipitate is washed, separated and dispersed in boiling water to which hydrochloric acid is added (1 part HCl to 3 parts moist precipitate and 10 parts water). The whole is then boiled and evaporated to dryness on a sand bath; this leads to partial decomposition of the compound with the formation of H_2WO_4. The barium B.T. obtained is again treated with water and a few drops of HCl, the solution filtered from H_2WO_4 and crystallized. The salt is obtained in the form of large square-octahedra.

Barium cis-B.T. is prepared by the action of $BaCO_3$ on sodium B.T. solution; the difficultly soluble barium trans-B.T. is precipitated leaving in solution sodium carbonate and the salt of the cis-acid, which crystallizes out on evaporation. Repeated recrystallization of the salt is required to obtain the barium B.T. in a pure state; its 27- and 29-hydrates are known.

In the first series of experiments we attempted to prepare barium B.T. from sodium B.T. directly. To achieve this, barium chloride was added to the original solution of the sodium salt in the amount calculated for the formation of the penta-substituted salt.

After 2-3 hours the precipitate of barium trans-B.T. obtained was filtered off and the filtrate, containing the barium salt of the cis-acid, was subjected to fractional crystallization; pure barium B.T. could not, however, be obtained by this method.

In the second series of experiments a mixture of cis- and trans-B.T. acids was separated from the sodium B.T. solutions with ether, and on treatment of the acid mixture with barium carbonate the soluble cis-B.T. salt was obtained. The extraction of the B.T. acid with ether is a difficult operation. It was established that the greatest yield of B.T. acid (75-90%) is obtained when the concentration of the sulfuric acid is 65% and the volume of it taken equals that of the original sodium B.T. solution. But even in these conditions the extraction of the complex is not always reproducible.

In the third series of experiments the synthesis of the sodium B.T. was carried out in sulfuric acid. The B.T. acid was extracted as the complex with ether as described for the preceding series of experiments, and mixed with water. The extraction of the complex under these conditions took place without decomposition.

In order to find the optimum conditions for the preparation of barium B.T., experiments were carried out in which the salts were separated from acid solutions of different concentration. In each experiment 25 ml sodium B.T. solution, 10 ml ether and 25 ml 65% H_2SO_4 were used for the extraction of the ether complex. The complex obtained was mixed with water, the acid neutralized with $BaCO_3$ to the formation of the 5-substituted salt and filtered from the precipitate of barium trans-B.T. The analysis of the filtrate indicated the relative concentrations $5BaO \cdot B_2O_3 \cdot 24WO_3$. The analysis results are given in Table 1.

In experiments 5 and 6 the solutions remained turbid after 2 recrystallizations, and on the following day (i.e. after 16-18 hours) a slight precipitate of H_2WO_4 had appeared in them (onset of decomposition). In experiments 3 and 4 the yield of salt was practically the same but the solutions were stable on prolonged standing. The solutions from experiments 3 and 4 were combined and evaporated on a boiling water bath; the crystals obtained were analysed to find the H_2O and BaO contents with the results H_2O – 12.44%, BaO – 12.26% (BaO calculated for the salt without water of crystallization 11.98%). The salt obtained corresponded to the formula $Ba_5H_8[B(W_2O_7)_6]_2 \cdot 46H_2O$.

TABLE 1

The Preparation of Barium B.T. Solutions

Specimen No.	Quantity of water (ml)	Solution obtained (g)	Concentration of oxides in solution (%)	Conc. of salt (g/100 g solution)
1	25	25	8.92	2.20
2	50	40	7.90	3.80
3	60	64	6.22	3.98
4	60	63	4.48	4.08
5	75	75	5.48	4.10
6	100	105	3.98	4.28

Three experiments were subsequently carried out on the preparation of barium B.T. in conditions similar to those of experiments 3 and 4. 200 ml of the original sodium B.T. solution was taken for each experiment; the ether complex obtained was mixed with 480 ml water. The acid obtained was neutralized with $BaCO_3$ and the solution filtered 18 hours after neutralization. The filtrates were evaporated to obtain the barium B.T. crystals. The results of the experiments carried out are given in Table 2.

The crystals obtained were mixed and analysed for BaO and H_2O content. Found %: H_2O 10.97; BaO 12.13. $Ba_5H_8[B(W_2O_7)_6]_2 \cdot 40\ H_2O$. Calculated %: H_2O 10.01; BaO 11.98.

From the results of the experiments carried out the following method is proposed for the preparation of barium B.T.: sulfuric acid (d 1.18) is added to a hot aqueous solution containing stoichiometric amounts of sodium tungstate and H_3BO_3 until faintly acid to congo red. The solution obtained is heated for 4 hours on a boiling water bath, keeping the volume constant, then left for 16-18 hours and carefully filtered. The B.T. acid is extracted from the filtrate with ether in the presence of 65% sulfuric acid. The ether complex is mixed with water, taken in the amount calculated to give an approximately 10% solution of the acid. Thus the ether complex isolated from 200 ml of original sodium B.T. solution, containing 50 g of B.T. acid, is mixed with 480 ml H_2O.

TABLE 2

The Preparation of Crystalline Barium B.T.

Specimen No.	Volume of solution (ml)	d^{20}	Amount of $BaCO_3$ taken for neutralization (g)	Yield of $Ba_5H_8[B(W_2O_7)_6]_2$ (%)
1	500	1.019	40	54.00
2	507	1.017	41	53.36
3	493	1.051	41	55.08

The acid is neutralized with $BaCO_3$ according to the equation:

$$2H_9[B(W_2O_7)_6] + 5BaCO_3 = Ba_5H_8[B(W_2O_7)_6]_2 + 5H_2O + 5CO_2$$

The barium salt of the trans-acid is insoluble and is precipitated; the solution is carefully filtered after 16-18 hours; the filtrate – a solution of barium cis-B.T. containing approximately 6% of the salt – is evaporated to isolate the crystals.

The yield of $Ba_5H_8[B(W_2O_7)_6]_2$ is 55% of the theoretical.

Analytical part. The analysis of barium B.T. consisted of the determination of H_2O, B_2O_3 and Ba.

For the water determination, a sample of 0.4-0.6 g of barium B.T. was placed in a porcelain or platinum crucible, 1-2 ml water was added, and the solution carefully evaporated to dryness in an air bath over a low flame; the crucible was then maintained at 300° for 30 minutes and ignited to constant weight with the naked flame of the burner. The loss in weight gave the amount of salt-forming water and water of crystallization in the salt sample taken.

For the BaO determination, a sample of approximately 1 g of salt was dissolved in 150 ml water and the Ba precipitated with 10% Na_2SO_4 solution, the precipitate left to stand for 16-18 hours and the $BaSO_4$ content determined in the usual way.

For the B_2O_3 determination a sample weighing 0.7-0.8 g was dissolved in 150 ml water. 30 ml of boiling 4% barium hydroxide solution was added to the solution, the precipitate left to stand for 5 minutes and filtered. The precipitate on the filter was washed with 50 ml water; the wash water was combined with the main filtrate and the solution obtained neutralized with 0.1 N hydrochloric acid to methyl orange; 30 ml of neutral glycerol diluted with water in the ratio 1:2 was then added, the whole left to stand for 15 minutes and the boric acid titrated with 0.1 N caustic soda using phenolphthalein indicator; the addition of glycerol (subsequent amounts 15 ml each) and the titration were continued until the addition of a portion of glycerol did not cause the pink coloration to disappear.

SUMMARY

1. A method for synthesizing sodium borotungstate under conditions employing stoichiometric amounts of H_3BO_3 and sodium tungstate has been worked out for the first time; the quantity of H_3BO_3 used is 100 times less than that used in the literature descriptions.

2. The method worked out for the preparation of barium cis-borotungstate enables this salt to be used for the synthesis of stable salts of cis-borotungstic acid.

3. The conditions for the ether extraction of B.T. acids and the method of analysing barium B.T. have been made more precise.

LITERATURE CITED

[1] Klein, Ann. chim. et phys. (5) 28, 350 (1883); Kahlbaum, Z. anorg. Chem. 29, 215 (1902); Copaux, Ann. chim. et phys. (8) 17, 217 (1908).

[2] Souchay, Ann. chim. et phys. (11) 20, 96 (1945).

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All-union Chemical Reagent Scientific Research Institute

A STUDY OF THE LAWS GOVERNING THE DISTRIBUTION OF ISOMORPHOUS COMPONENTS ON CRYSTALLIZATION FROM AQUEOUS SOLUTION, INVOLVING THE USE OF RADIOACTIVE INDICATORS

II. THE STUDY OF THE DISTRIBUTION OF THE COMPONENTS IN THE SYSTEM $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O - ZnSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O - H_2O$ Using the Radioactive Indicator Zn^{65}

N. I. Silantyeva and G. I. Gorstein

The system $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O - ZnSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O - H_2O$ has been studied at macroconcentrations of both isomorphous components [1]. From the experimental data from this for 8.5° we have calculated the distribution equilibrium coefficients for the zinc salt relative to the iron salt. The calculation was carried out using the formula:

$$D_{Zn/Fe} = c_{ZnSP}/c_{FeSP} : c_{Zn\,MS}/c_{Fe\,MS},$$

where $c_{Zn\,SP}$ and $c_{Zn\,MS}$ – concentration of the zinc salt in the solid phase and in the mother solution, $c_{Fe\,SP}$ and $c_{Fe\,MS}$ – corresponding data for the iron salt.

It turned out that the value of the distribution coefficient for the zinc salt $D_{Zn/Fe}$ varies from 1.5 to 4.2 as the concentration of the zinc salt in the salt fraction of the mother solution changes from 9 to 80%. It follows from this that according to the experimental data from [1] the system deviates considerably from ideal behavior. We first of all made a study of the distribution equilibrium of microconcentrations of added zinc salt on crystallization of $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ from aqueous solutions. Experiments were carried out at 0, 10, 20, 30° using the radioactive indicator Zn^{65}. The experimental method and the calculation of the results are described earlier [2].

The concentration of $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ in crystals and solutions was determined by titration with 0.1 N potassium permanganate solution. The experimental results are given in Table 1, from the data in which it can be seen that the value of the distribution equilibrium coefficient for added Zn in the crystallization of $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ varies little with temperature in the range 0 to 30°. Its mean value at 0° – 4.7, at 10° – 5.0, at 20° – 4.3 and at 30° – 4.3. The values found by us for the Khlopin constant $D_{(Zn)/Fe}$ differ markedly from the values of the distribution coefficient $D_{Zn/Fe}$ calculated from the experimental data in [1] for the region of low zinc salt concentration, but are close to the values of the distribution constants for the region of high concentrations of this salt. This led us to undertake a study of the equilibrium distribution of the components at macroconcentrations.

The experiments were carried out at 20° in view of the fact that other systems [6-8] have also been studied by us at this temperature. In part of the experiments the macroconcentrations of the zinc salt in the crystals and solutions were determined using radioactive indicator methods. A zinc salt previously brought to a definite specific activity with the radioactive isotope Zn^{65} was used. The iron salt concentration was determined by titration with potassium permanganate. The concentration of zinc salt in the crystals and mother solutions was determined by titration with potassium ferrocyanide using ammonium molybdate as external indicator. The iron was previously removed as the hydroxide after oxidation by heating with hydrogen peroxide. The amount of zinc lost with the ferric hydroxide precipitate was checked using radioactive indicator methods: before the analysis was carried out, the radioactive indicator Zn^{65} was added to the solution, and from a comparison of the activities of the original solution and the solution obtained by dissolving the ferric hydroxide precipitate, after washing, in dilute sulfuric acid, the degree of coprecipitation of traces of zinc by the ferric hydroxide was calculated. Appropriate corrections were made in the analysis data. In this way the lengthy operations involving double precipitation of the ferric hydroxide with careful washing, as is necessary in the usual determination of a zinc salt in the presence of iron salts, was avoided. In some experiments, the iron, after preliminary oxidation with hydrogen peroxide and separation as the hydroxide, was determined photocolorimetrically as the sulfosalicylic complex.

TABLE 1

The Equilibrium Distribution for Microconcentrations of Zinc Salt in the Crystallization of $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ at Different Temperatures

Temperature	Concentration of added zinc (% by weight)	$FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ (% by weight)			Number of impulses for 1 g per minute				Degree of crystallization of the iron salt α	$D_{(Zn)/Fe}$
		In the crystals	In the mother solution	In the original solution	Of the crystals	Of the mother solution	Of the solid phase	Of the salt fraction of the mother solution		
0	0.1	95.24	20.88	24.35	298	14.9	316	71.3	0.18	4.4
0	0.1	96.76	20.29	24.10	142	6.37	148	31.4	0.20	4.7
0	0.1	97.16	20.30	24.10	145	6.49	148	31.9	0.20	4.6
0	0.16	94.88	20.81	26.19	578	27.0	616	130	0.26	4.7
0	0.18	94.99	20.46	25.19	259	11.4	278	55.7	0.24	4.9
10	0.1	95.46	25.31	31.91	440	21.9	467	86.6	0.27	5.4
10	0.5	91.14	24.62	28.62	517	32.0	581	129	0.18	4.5
10	0.5	88.84	24.69	28.62	543	30.2	632	122	0.18	5.2
10	1.0	80.10	24.75	29.06	419	28.8	560	115	0.19	4.8
20	<0.01	97.20	29.40	34.80	296	20.2	307	68.9	0.22	4.1
20	<0.01	97.09	28.86	36.36	83.8	5.96	87.1	20.6	0.29	4.2
20	0.01	95.60	28.90	35.52	283	19.6	301	67.8	0.32	4.4
20	0.1	93.60	28.64	33.16	281	20.4	307	71.2	0.21	4.3
20	0.2	94.62	28.66	—	78.1	5.08	84.1	17.7	—	4.7
20	0.3	90.74	28.24	32.15	363	26.1	407	92.6	0.17	4.4
30	0.1	93.30	32.45	41.61	271	22.4	299	68.9	0.32	4.3
30	0.1	94.54	32.43	41.61	272	22.4	294	69.0	0.32	4.3
30	0.2	94.06	32.40	38.71	291	23.4	317	72.2	0.28	4.4
30	0.2	92.54	32.56	38.71	283	24.1	315	73.9	0.20	4.3

The experimental results are given in Table 2 and in Figures 1 and 2.

As can be seen from the data in Table 2, the value of $D_{Zn/Fe}$ at 20° changes from 4.1 to 3.5 as the concentration of zinc salt in the salt fraction of the mother solution increases form 3.0 to 95.6%. In addition the system is ideal in two wide regions at the extremes of the distribution diagram. As the concentration of the zinc salt in the solid phase changes from 0 to 77%, the value of $D_{Zn/Fe}$ remains constant at 4.1.

It became of interest to examine to what extent the added zinc was coprecipitated with the crystals of $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ in conditions analogous to those of the normal crystallization process in industrial apparatus with stirring. With this aim we carried out several experiments to extablish the value of the practical distribution coefficient ($D_{pr.}$) for microconcentrations of zinc impurity in the slow polythermal crystallization of $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$, using the radioactive indicator Zn^{65}. The concentration of added zinc in all experiments was 0.1 %. The crystallization was carried out by evenly cooling solutions of $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ with uninterrupted stirring for 5-8 hours. The results of these experiments are given in Table 3. As can be seen from the data in Table 3, the value of D_{pr} obtained is much greater than $D_{Zn/Fe}$ for the final crystallization temperature: $D_{pr.} = 12\text{-}28$, while $D_{Zn/Fe} = 4.2\text{-}4.8$.

It has been shown by one of us [3] that the coprecipitation of impurities in polythermal crystallization is determined by two factors.

a) By the magnitude of the relative supersaturation of the solution r at each moment of the crystallization. The relationship between the practical differential (surface) distribution coefficient $\lambda_{pr.}$, the relative supersaturation r and the value of the equilibrium differential distribution coefficient of the microcomponent is given by the approximate formula [3]:

TABLE 2

Equilibrium in the System $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O - ZnSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O - H_2O$ at 20°

Analysis results (% by weight)						Concentration (% by weight)				Total degree of crystallization α total	$D_{Zn\,Fe}$
Of the crystals		Of the mother solution		Of the original solution		In the solid phase		In the salt fraction of the mother solution			
$FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$	$ZnSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$	$FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$	$ZnSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$	$FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$	$ZnSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$	$FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$	$ZnSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$	$FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$	$ZnSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$		
1.25	91.6	0.65	14.2	0.75	23.5	1.30	98.7	4.40	95.6	0.45	3.5
1.28	91.3	0.68	14.3	0.75	23.5	1.30	98.7	4.60	95.4	0.45	3.5
6.02	78.4	3.11	12.1	3.67	21.7	6.70	93.3	20.5	79.5	0.46	3.5
6.17	86.6	3.13	12.0	3.67	21.7	6.45	93.6	20.7	79.3	0.46	3.5
10.03	81.8	5.06	11.9	5.66	18.9	10.6	89.6	29.9	70.1	0.36	3.5
9.41	78.2	5.15	11.8	5.66	18.9	10.6	89.4	30.4	69.6	0.37	3.7
14.30	73.8	7.04	10.0	7.76	15.5	15.6	84.4	41.7	58.3	0.32	3.8
22.16	74.4	10.30	8.82	10.90	11.9	22.7	77.3	53.9	46.1	0.23	4.0
38.74	59.1	15.33	5.92	21.51	10.6	39.4	60.6	72.2	27.8	0.43	4.0
57.00	35.7	20.42	3.11	21.92	3.95	60.9	39.1	86.8	13.2	0.12	4.1
84.71	10.8	27.16	0.85	32.41	2.08	88.5	11.5	97.0	3.0	0.26	4.1

TABLE 3

Values of $D_{pr.}$ for Added Zn in the Polythermal Crystallization of $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$

Temperature		$FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ (% wt.)			Number of impulses for 1 g per minute				Degree of crystallization of main substance α	$D_{pr.}$	Remarks
Initial	Final	In the crystals	In the mother solution	In the original solution	Of the crystals	Of the mother solution	Of the solid phase	Of the salt fraction of the mother solution			
30°	0°	93.20	20.50	32.32	293	5.48	320	26.7	0.46	11.9	Crystals appeared after 1 hour at 24°
30	0	93.00	20.49	32.32	299	5.20	319	25.3	0.46	12.6	Crystals appeared after 1.5 hours at 21°
30	0	94.52	20.16	31.61	531	8.47	559	42.0	0.45	13.3	Crystals appeared after 80 minutes at 24.5°
30	0	94.80	20.13	31.61	524	8.40	560	41.7	0.45	13.4	
55	20	89.12	28.70	46.70	150	1.80	177	6.27	0.54	28.2	Crystals appeared after 15 minutes at 55°
55	20	94.74	28.74	46.70	161	2.00	174	6.95	0.54	25.0	

$$\lambda_{pr.} = \frac{r \cdot \lambda}{\lambda(r-1)+1}. \qquad (1)$$

The influence of the value of r is shown very distinctly when λ is significantly greater than unity.

b) By the magnitude of the degree of crystallization of the main substance towards the end of the crystallization $-\ \alpha$.

The value of the mean practical distribution coefficient for the microcomponent in cases where the value of $\lambda_{pr.}$ changes little in the crystallization temperature range, is given by the formula:

$$D_{pr.} = \frac{(1-\alpha)^{-\lambda_{pr.}} - 1}{\alpha}(1-\alpha). \qquad (2)$$

We give the calculation of the value of $D_{pr.}$ for the polythermal crystallization of $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ according to formulas (1) and (2) for the conditions of the first four experiments (Table 3).

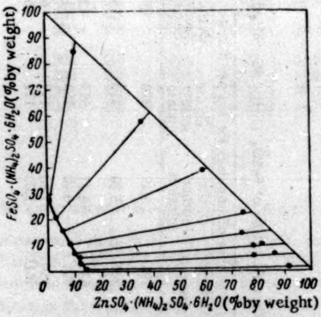

Fig. 1. Equilibrium composition diagram.

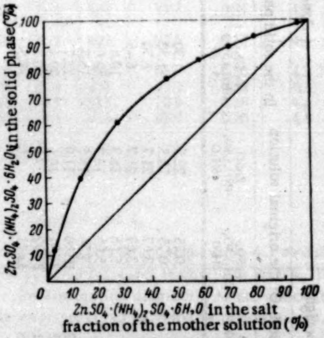

Fig. 2. Component distribution diagram.

In these experiments the first crystals appeared from 1–1.5 hours after the commencement of cooling, when the solution temperature had reached 24°. The concentration of a saturated solution of the double salt at this temperature is 30% $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$. Since the concentration of the original solution was 31.6–32.3% the relative supersaturation of the solution relative to the main material at the moment when the first crystals separated was 1.05–1.08 (supersaturation 5–8% relative to the saturated solution). The mean value of the relative supersaturation in the complete range of the polythermal crystallization may be taken as equal to 1.03. The value of λ in the range 0 to 30° varies little with temperature and may be taken as having a mean value of 4.5. The mean value of the practical differential distribution coefficient, according to formula (1), is then $\lambda_{pr.} = 4.1$. The value of the mean practical distribution coefficient of the added Zn, calculated according to formula (2), is $D_{pr.} \doteq 12$. The calculated result thus agrees well with the experimental data obtained from the slow polythermal crystallization with final temperature 0°.

We give now the calculation of the extent of the increase in concentration of the added Zn in the crystals and the extent of the decrease in its concentration in the mother solutions in the polythermal crystallization of $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ with final temperature 20°. The value of $D_{pr.}$ found by us for these crystallization conditions with $\alpha = 0.54$ equals 25–28. Let us take the mean value 26. The coefficient of isomorphous lattice adsorption in the solid phase (the coefficient of increase in concentration of added Zn in the solid phase) is found from the formula [4, 5]:

$$\varphi^{*}_{SP}=\frac{D}{\alpha D+1-\alpha}=2.1.$$

The corresponding coefficient for the content of added Zn in the mother solution φ_{MS}** is given by the formula [4,5]:

$$\varphi_{MS}=\frac{1}{\alpha D+1-\alpha}=0.081.$$

The reciprocal of φ_{MS} is the factor by which the concentration of added Zn in the mother solution is decreased. Thus for the crystallization of Mohr's salt in conditions corresponding to those of the industrial process, an approximately 2-fold increase in concentration of added Zn in the solid phase takes place, while a 12-fold decrease takes place in its concentration in the mother solution.

SUMMARY

1. A study has been made of the equilibrium distribution of microconcentrations of added Zn in the crystallization of the double sulfate of iron and ammonia in the temperature range 0 to 30°.

2. It has been established that the value of the equilibrium distribution coefficient for microconcentrations of added Zn – the Khlopin constant $D_{(Zn)/Fe}$ – changes little with temperature and at 0° equals 4.7, at 10° – 5.0, at 20° – 4.3 and at 30° – 4.3.

3. A study has been made of the equilibrium in the system

$$FeSO_4\cdot(NH_4)_2SO_4\cdot 6H_2O - ZnSO_4\cdot(NH_4)_2SO_4\cdot 6H_2O - H_2O$$

at 20° with macroconcentrations of the components for the complete range of component concentration. It has been established that the distribution coefficient of the zinc salt $D_{Zn/Fe}$ in this system varies from 4.1 to 3.5.

4. The presence of two wide regions of ideal behavior in the system studied has been established at the extremes of the equilibrium diagram.

5. Values have been found for the mean practical distribution coefficients for added Zn in the slow polythermal crystallization of $FeSO_4\cdot(NH_4)_2SO_4\cdot 6H_2O$ and it has been shown that the results obtained experimentally correspond to the theoretical data.

6. The extent of the increase in concentration of added Zn in the solid phase and its decrease in the mother solution in the polythermal crystallization of $FeSO_4\cdot(NH_4)_2SO_4\cdot 6H_2O$ from aqueous solution in conditions corresponding to those of the industrial process has been calculated.

LITERATURE CITED

[1] Ostersetzerown, Roczniki Chem 6, 679 (1926).

[2] G. I. Gorstein, N.I. Silantyeva, J. Gen. Chem. 26, 1821 (1956) (T.p.2033). ***

[3] G. I. Gorstein, Works of the Chemical Reagent Institute (IREA) (1951) No. 20, 44.

[4] G. I. Gorstein, Works of the Chemical Reagent Institute (IREA) (1951) No. 20, 40.

[5] G. I. Gorstein, Chem. Ind. USSR 1948, No. 3.

[6] G. I. Gorstein, N. I. Silantyeva, J. Gen. Chem. 23, 1290 (1953) (T.p. 1355). ***

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* The quantity φ_{SP} is the ratio of the concentration of impurity in the solid phase to its concentration in the original salt being crystallized.

** The quantity φ_{MS} is the ratio of the concentration of impurity in the salt fraction of the mother solution to its concentration in the original salt.

*** T.p.= C.B. Translation pagination.

[7] G. I. Gorstein, N. I. Silantyeva, J. Gen. Chem. 24, 29 (1954) (T.p. 27).*

[8] G. I. Gorstein, N. I. Silantyeva, J. Gen. Chem. 24, 201 (1954) (T.p. 201).*

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Chemical Reagent Institute

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* T.p. = C.B. Translation pagination

A STUDY OF COMPLEX FORMATION IN SOLUTIONS OF TERNARY SYSTEMS BY THE METHODS OF PHYSICO-CHEMICAL ANALYSIS

VII. THE SYSTEM $AlBr_3-(C_2H_5)_2O-C_6H_6$

E. Ya. Gorenbein and V. L. Pivnutel

The study of the reaction of aluminum bromide with ethyl ether has shown that these components form a compound of equimolecular composition [1], and this has been confirmed by a study of the reaction of $AlBr_3$ with $(C_2H_5)_2O$ in benzene as solvent using the cryoscopic method [2]. The study of the same subjects in ethylene dibromide as solvent using electrical conductivity methods, however, has provided evidence for suggesting that these materials form two complex compounds:

$$AlBr_3 \cdot (C_2H_5)_2O \text{ and } Al_2Br_6 \cdot (C_2H_5)_2O \ [3]$$

The study of the reaction of $AlBr_3$ with nitrobenzene in ethylene dibromide [4] and ethyl bromide as solvents has shown that $AlBr_3$ and $C_6H_5NO_2$ form three complex compounds; it was also established that by measuring the viscosity it is possible to find the compound in the solution which is the best conductor of electricity [4]. We undertook the present study in order to clarify the number of compounds formed between $AlBr_3$ and ethyl ether and to examine the applicability of the above-mentioned rule.

The aluminum bromide was synthesized by the action of bromine on aluminum turnings. The product was distilled twice and stored in sealed ampoules. The benzene–cryoscopic material–was first dried over fused calcium chloride, distilled, dried a second time over metallic sodium, and then distilled into ampoules which were sealed as soon as they were full. The ethyl ether was prepared as described in [2]. The dissolution of the ether in the benzene solution of aluminum bromide was accompanied by the evolution of heat. The color of the solution varied with the molecular ratio of aluminum bromide and ethyl ether. When the ether was present in excess, the solution was colorless, with the bromide in excess, the solution was a straw-yellow color (the latter solution was the more stable). When the solution containing excess ether was preserved for some time it at first became darker and then turned black.

For the investigation, the solutions were prepared so that the ratio of the total number of moles of $AlBr_3 + (C_2H_5)_2o$ to 1 mole of the solvent (benzene) equalled 0.150 ± 0.001.

The electrical conductivity, viscosity and density of the solutions were measured at 15, 20 and 25°. The method for preparing the solutions and the technique of taking the measurements has been described earlier [5]. In the measurement of the electrical conductivity, difficulties arose as a result of the reaction of the ether with bromine. In the cases where the aluminum bromide contained traces of bromine, the electrical conductivity rose sharply, and these points are not given in the curve. For this reason the freshly-prepared aluminum bromide was carefully protected from the action of light. Sometimes we carried out the following procedure: a piece of metallic aluminum was placed in the ampoule before it was filled with $AlBr_3$; the molten mass was then heated for a short time on a sand bath before use and only then was the $AlBr_3$ taken for the experiment. In these cases no scatter of the points was observed. The results of the measurement of solution viscosity and density are given in Table 1 and the specific conductivity in Table 2.

Figure 1 shows the variation in viscosity and specific conductivity with the concentration of the components $AlBr_3$ and $(C_2H_5)_2O$, the total number of moles of these being taken as 100%. The points lying on the ordinate axes correspond to the properties of the binary systems $AlBr_3-C_6H_6$ and $(C_2H_5)_2O-C_6H_6$. It can be seen from the curves (I) in the given figure that as the concentration of $AlBr_3$ increases, the specific conductivity at first rises and reaches a maximum at about 50 mole %, after which it decreases sharply, passes through a minimum and again rapidly increases to reach a second maximum. The first maximum corresponds approximately to the composition of the compound $AlBr_3 \cdot (C_2H_5)_2O$; the minimum gives no grounds for asserting that a compound of other composition is present in the solution. The second maximum corresponds to the composition of the compound $Al_2Br_6 \cdot (C_2H_5)_2O$.

TABLE 1

Viscosity and Density of the System $AlBr_3-(C_2H_5)_2O-C_6H_6$

$AlBr_3$ content (mole %)	15°		20°		25°	
	d_4^t	$\eta \cdot 10^2$	d_4^t	$\eta \cdot 10^2$	d_4^t	$\eta \cdot 10^2$
100	1.1509	0.940	1.1450	0.871	1.1392	0.800
80.09	1.1010	0.949	1.0943	0.876	1.0886	0.808
69.00	1.0704	0.954	1.0650	0.873	1.0595	0.794
60.81	1.0486	0.948	1.0432	0.869	1.0379	0.799
55.72	1.0343	0.937	1.0284	0.866	1.0232	0.786
49.46	1.0168	0.906	1.0115	0.834	1.0063	0.765
46.52	—	—	1.0014	0.825	0.9968	0.758
44.64	1.0036	0.874	0.9959	0.804	0.9908	0.738
38.75	0.9836	0.846	0.9801	0.774	0.9740	0.717
28.09	0.9488	0.780	0.9438	0.730	0.9385	0.670
22.42	0.9310	0.769	0.9258	0.692	0.9205	0.638
0	0.8592	0.639	0.8543	0.589	0.8495	0.545

TABLE 2

Specific Conductivity of the System $AlBr_3-(C_2H_5)_2O-C_6H_6$

$AlBr_3$ content (mole %)	15°	20°	25°
	$\varkappa \cdot 10^4$	$\varkappa \cdot 10^4$	$\varkappa \cdot 10^4$
100	—	—	—
90.18	0.099	0.099	0.099
80.09	0.243	0.249	0.250
75.27	0.497	0.524	0.553
69.00	0.740	0.813	0.834
65.04	0.999	1.037	1.064
62.64	1.096	1.142	1.178
57.42	0.958	0.970	0.986
56.86	0.934	0.957	0.972
55.10	0.520	0.525	0.553
54.15	0.489	0.496	0.498
53.20	0.343	0.355	0.375
50.35	0.692	0.743	0.784
49.46	0.712	0.777	0.807
46.52	0.683	0.727	0.747
44.64	0.641	0.681	0.721
38.75	0.489	0.518	0.549
28.09	0.161	0.170	0.184
22.42	0.088	0.093	0.092
0	—	—	—

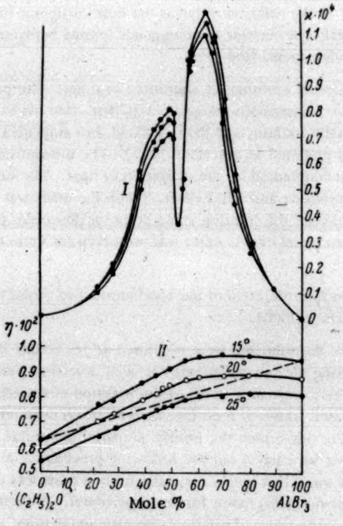

Fig. 1. The variation of viscosity and specific conductivity in the system $AlBr_3-(C_2H_5)_2O-C_6H_6$ with the concentrations of the components.

I) specific conductivity curves, II) viscosity curves.

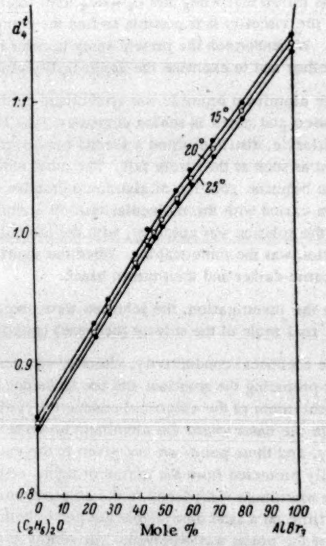

Fig. 2. Relationship between the density in the system $AlBr_3-(C_2H_5)_2O-C_6H_6$ and the concentration of the components.

The viscosity curves (II) show a sloping maximum. If a straight line is drawn connecting the viscosities of the binary systems [$AlBr_3-C_6H_6$ and $(C_2H_5)_2O-C_6H_6$], then the greatest deviation from the straight line coincides with the second conductivity maximum. This confirms the rule according to which the viscosity curves show the compound, formed from the two nonelectrolytes, which best conducts current.

Figure 2 shows the relationship between the solution density and the concentration of the components $AlBr_3$ and $(C_2H_5)_2O$. The break in the straight line corresponds to the compound of equimolecular composition.

Thus the density, the cryoscopic studies [2] and the first maximum on the conductivity curve indicate that aluminum bromide forms with ethyl ether the compound of composition $AlBr_3 \cdot (C_2H_5)_2O$, while the viscosity and the second conductivity maximum indicate the compound of composition $Al_2Br_6 \cdot (C_2H_5)_2O$. Consequently, the results obtained by us give grounds for asserting that aluminum bromide forms with ether not one complex compound, as was previously thought, but two, whose structures are, in all probability, similar to those given by us earlier [4]. It should be noted that compounds of similar composition have been established for aluminum bromide with nitrobenzene [4], dioxane [6] and pyridine [7].

SUMMARY

1. A study has been made of the viscosity, electrical conductivity and density of the section of the system $AlBr_3-(C_2H_5)_2O-C_6H_6$ corresponding to a molar ratio of $AlBr_3 + (C_2H_5)_2O$ to benzene (the solvent) of 0.15 at temperatures of 15, 20 and 25°.

2. It has been established that in the experimental conditions taken aluminum bromide forms with ethyl ether the two complex compounds $AlBr_3 \cdot (C_2H_5)_2O$ and $Al_2Br_6 \cdot (C_2H_5)_2O$.

3. A demonstration has been given of the applicability to the present case of the rule which states that if two substances which are not electrolytes form two or more compounds, then the presence of the compound which best conducts electric current will be reflected in the viscosity curves.

LITERATURE CITED

[1] V. A. Plotnikov, M. L. Kaplan, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1948, 256; V. A. Plotnikov, J. Russ. Chem. Soc. 39 163 (1907); Nickles, Compt.rend. 52, 869 (1861).

[2] E. Ya. Gorenbein, V. L. Pivnutel and I. A. Gerasun, J. Gen Chem. 23, 544 (1953) (T.p. 563)*.

[3] E. Ya. Gorenbein, J. Gen. Chem. 24, 1507 (1954) (T.p. 1493)*.

[4] E. Ya. Gorenbein, J. Gen. Chem. 24, 1710 (1954) (T.p. 1685)*.

[5] E. Ya. Gorenbein, J. Gen. Chem. 23, 1273 (1953) (T.p. 1339)*.

[6] I. A. Sheka, K. F. Karlysheva, J. Gen. Chem. 21, 833 (1951) (T.p. 915)*.

[7] V. A. Plotnikov, J. Gen. Chem. 1, 823 (1931).

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Kiev Veterinary Institute and the Institute of Physiology of the Ukrainian SSR Academy of Sciences

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* T.p. = C.B. Translation pagination.

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Figure 2 [illegible]

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THE COMPOSITION OF BORATES IN AQUEOUS SOLUTION

E. M. Schwarz and S. G. Vimba

Up to the present only the composition of the alkali metal borates in aqueous solution has been studied. The experimental material obtained, however, has led to contradictory interpretations. Thus early investigators, who studied the electrical conductivity and cryoscopic behavior of the alkali metal borates, considered that in dilute aqueous solutions the tetraborate ion is stable [1,2[. Carpeni, from data on the potentiometric titration of boric acid with caustic alkali solutions of different concentrations, states that in dilute aqueous borate solutions there is only one equilibrium: pentaborate ($HB_5O_9^{--}$) – monoborate ($H_2BO_3^-$) [3-6]. Dibasic pentaborates however, although prepared, have only been obtained under increased pressure and at high temperature [7, 8]. From the difficulty of preparing these compounds it is highly improbable that these ions predominate in solution. On these grounds, Souchay disputed Carpeni's conclusions [9, 10] and considered that in aqueous alkali metal borate solutions the borate ions $B_5O_8^-$ and $B_4O_7^{2-}$ could exist, and that at low concentrations these were hydrolyzed to monoborate ion BO_2^- and H_3BO_3 [11].

All these hypotheses cannot be extended to aqueous solutions of the alkaline earth and heavy metal borates, since these borates are of a completely different type, requiring special study. In recent years many borates of magnesium, calcium, barium, lead, cadmium, manganese, cobalt and nickel, including borates belonging to the class of double salts, with up to twelve boron atoms in the molecule, have been synthesized [15-26]; it therefore became of interest to examine the composition of the species into which the different borates dissociate on going into solution.

We have carried out systematic measurements of the coefficient i and the molecular conductivity μ_ν of aqueous borate solutions. The freezing point depressions were measured by the well-known Beckmann method. The molar conductivity was determined by Kohlrausch's method, aqueous borate solutions and solutions of borates in 2 and 3% boric acid being studied. The molar conductivity at infinite dilution was found by extrapolation (some examples are given in Figure 1). From this in turn the ionic conductance ν of the borate anion was calculated [12].

The composition of borates in aqueous solution varies with the borate concentration and is affected by the presence or absence of certain added materials, particularly boric acid. The data given refer only to dilute borate solutions with concentrations below 0.01 M. The composition of the borates in aqueous solution depends also on the cation, or, more accurately, on the strength of the base formed by the cation in question. For this reason three groups of borates were studied.

1. The borates of the alkali metals and ammonia. The ionic conductance of the borate anion in alkali metal borate solutions at infinite dilution fluctuates around the value 39 ohm$^{-1}\cdot$cm^2 (Table 1). The ionic conductance of $H_2BO_3^-$, determined indirectly, is known from the literature and is equal to 36.8 ohm$^{-1}\cdot$cm^2 [13]. The cryoscopic coefficient for monoborate solutions at concentrations from 0.04 to 0.01 M, according to Menzel's data, equals 1.5-1.9 [2].

Consequently, the alkali metal monoborates in aqueous solutions behave as binary electrolytes:

$$MeBO_2 \rightleftharpoons Me^+ + BO_2^-.$$

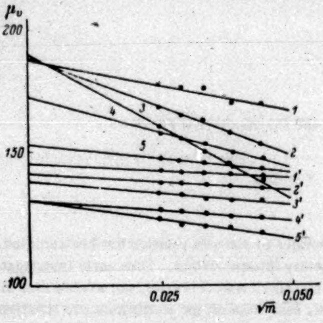

Fig. 1. The variation with dilution of the electrical conductivity of alkaline earth borate solutions.

1 — $SrB_6O_{10} \cdot 5H_2O$, *1'* — $SrB_2O_4 \cdot 4H_2O$ in 3% H_3BO_3, *2* — $CaB_6O_{10} \cdot 5H_2O$, *2'* — $CaB_6O_{10} \cdot 5H_2O$ in 3% H_3BO_3, *3* — $MgB_2O_4 \cdot 3H_2O$, *3'* — $SrB_6O_{10} \cdot 5H_2O$ in 3% H_3BO_3, *4* — $MgB_6O_{10} \cdot 7.5H_2O$, *4'* — $MgB_6O_{10} \cdot 7.5H_2O$ in 3% H_3BO_3, *5* — $BaB_2O_4 \cdot 4H_2O$ in 3% H_3BO_3, *5'* — $MgB_2O_4 \cdot 3H_2O$ in 3% H_3BO_3.

The formula of the monoborate ion has until recently remained an open question; certain authors have ascribed to it the formula $B_2O_4^{2-}$. Only very recently a work has appeared in which borate solutions have been studied using the Raman spectra. The results have shown that the ions $B(OH)_4^-$, with symmetrical structure, are formed in solution, i.e. ions which are essentially $BO_2^- \cdot 2H_2O$ [28].

The tetraborates of sodium and potassium in aqueous solution at concentrations 0.04-0.01 M have the cryoscopic coefficient 5.4-6, while that of the pentaborates varies from 3.9-6 (Table 2). The ionic conductance of the borate ion in these solutions, as in the monoborate solutions, is approximately equal to 39 ohm^{-1}·cm^2. All this points to the hydrolysis of the pentaborate and tetraborate ions in dilute aqueous solutions to the monoborate ion with the separation of boric acid:

$$Me_2B_4O_7 + 3\,H_2O \rightleftarrows 2\,Me^+ + 2\,BO_2^- + 2\,H_3BO_3,$$

$$2\,MeB_5O_8 + 9\,H_2O \rightleftarrows 2\,Me^+ + B_4O_7^{--} + 6\,H_3BO_3$$

$$B_4O_7^{--} + 3\,H_2O \leftrightarrows 2\,BO_2^- + 2\,H_3BO_3.$$

The addition of boric acid to alkali metal borate solutions results in a) the retardation of the hydrolysis of the pentaborate ion, and b) the combination of the excess boric acid with the monoborates and tetraborates, by which they are converted into more acidic polyborates. This is indicated by the following facts: 1) the identical ionic conductance of tetraborates, monoborates and pentaborates in a solution of 3% boric acid, approximately equal to 15 ohm^{-1}·cm^2 (Table 3) (the decrease in the ionic conductance of the anion corresponds to an increase in its size); 2) the cryoscopic coefficient of alkali metal tetraborate solutions decreases on dilution, i.e. on the dilution of 2% boric acid to a value less than unity (Table 4). We suggest that the ion formed in 3% boric acid solution is the pentaborate ion $B_5O_8^-$:

$$MeBO_2 + 4H_3BO_3 \rightleftarrows Me^+ + B_5O_8^- + 6\,H_2O$$

$$Me_2B_4O_7 + 6\,H_3BO_3 \rightleftarrows 2\,Me^+ + 2\,B_5O_8^- + 9\,H_2O.$$

This hypothesis is based on the following considerations: 1) it is known that when potassium pentaborate is dissolved in 3% boric acid solution, a precipitate of potassium pentaborate is obtained after a certain period of time; 2) when the molar conductivity of alkali metal pentaborate solutions in 3% boric acid was measured at dilutions of 32:1 and 1024:1, in all cases a difference in equivalent conductivities close to 11 was obtained, which indicates that the anion formed is monobasic and therefore cannot be $B_4O_7^{2-}$ or $HB_5O_9^{2-}$, as suggested by Carpeni.

2. The borates of the alkaline earth metals and magnesium. Only one work is known in the literature on the potentiometric titration of boric acid with barium hydroxide in the presence of glycerol [14]. The authors detected sharp potential jumps at B_2O_3 / BaO ratios of 1,2,3,4,8. The borates of the alkaline earth metals differ markedly in their dissociation in aqueous solution from the borates of the alkali metals. Thus the diborates of barium, strontium and calcium, which may be regarded as the analogs of the alkali metal monoborates, differ from the latter in that the electrical conductivity increases with dilution and the graph of the relationship between μ_v and $\sqrt{m}$ has the form of a concave curve (Figure 2).

TABLE 1

The Ionic Conductance of the Borate Ion in Aqueous Alkali Metal Borate Solutions

	$LiBO_2 \cdot 8H_2O$	$NaBO_2 \cdot 4H_2O$	$KBO_2 \cdot 2H_2O$	$K_2B_4O_7 \cdot 4H_2O$	$Na_2B_4O_7 \cdot 10H_2O$	$Li_2B_4O_7 \cdot 3H_2O$	$KB_5O_8 \cdot 4H_2O$	$NaB_5O_8 \cdot 5H_2O$	$LiB_5O_8 \cdot 5H_2O$
μ_∞	79	90	112	120	184	159	108	88	73
v_∞	40.3	40.9	39.0	36.5	40.3	40.8	34.5	37.9	34.3

TABLE 2

The Cryoscopic Coefficients of Tetraborates and Pentaborates in Aqueous Solution

$K_2B_4O_7 \cdot 4H_2O$		$Na_2B_4O_7 \cdot 10H_2O$		$KB_5O_8 \cdot 4H_2O$		$NaB_5O_8 \cdot 5H_2O$	
m	*i*	*m*	*i*	*m*	*i*	*m*	*i*
0.035	5.39	0.075	4.52	0.100	3.88	0.100	4.08
0.023	5.41	0.056	4.99	0.075	4.16	0.075	4.44
0.018	5.55	0.042	5.57	0.056	4.56	0.056	4.87
0.014	5.67	0.032	6.09	0.042	4.74	0.042	5.25
0.012	5.79	0.024	6.62	0.032	5.04	0.032	5.48
				0.024	5.49		
				0.018	5.94		

TABLE 3

The Ionic Conductance of the Borate Ion in Solutions of Alkali Metal Borates in 3% Boric Acid

	$LiBO_2 \cdot 8H_2O$	$NaBO_2 \cdot 4H_2O$	$KBO_2 \cdot 2H_2O$	$NaB_5O_8 \cdot 5H_2O$	$KB_5O_8 \cdot 4H_2O$	$NH_4B_5O_8 \cdot 4H_2O$	$LiB_5O_8 \cdot 5H_2O$	$Na_2B_4O_7 \cdot 10H_2O$	$K_2B_4O_7 \cdot 4H_2O$	$Li_2B_4O_7 \cdot 3H_2O$
μ_∞	56.0	65.5	88.0	67.0	86.5	89.0	56	129.0	177.5	113.0
v_∞	17.3	15.4	14.5	16.9	13.0	14.6	17.3	14.4	15.2	17.8

Curves of this shape can only indicate that these borates are completely hydrolysed on dilution.
$Me(BO_2)_2+4H_2O \rightleftharpoons Me^{++} + 2OH^- + 2H_3BO_3$.

Sure enough, the cryoscopic constant of these solutions, too, changes from 4 to 5 at concentrations 0.01-0.005 M.

TABLE 4

The Cryoscopic Coefficients of Alkali Metal Tetraborates in Solution in 2% H_3BO_3

$K_2B_4O_7 \cdot 4H_2O$		$Na_2B_4O_7 \cdot 10H_2O$		$(NH_4)_2B_4O_7 \cdot 4H_2O$	
m	*i*	*m*	*i*	*m*	*i*
0.600	1.17	0.100	1.26	0.100	1.47
0.088	0.99	0.088	1.16	0.075	1.42
0.031	0.96	0.064	1.16	0.056	1.31
0.025	0.88	0.051	1.14	0.045	1.27
		0.041	0.81	0.036	1.22
		0.033	0.92	0.027	1.08

When the hexaborates of the alkaline earth metals and magnesium are considered, it was found possible to measure the electrical conductivity in aqueous solution only for $MgB_6O_{10} \cdot 7.5H_2O$, $SrB_6O_{10} \cdot 5H_2O$, $CaB_6O_{10} \cdot 5H_2O$; barium hexaborate is quite insoluble. The ionic conductance of the borate anion is approximately 34 $ohm^{-1} \cdot cm^2$. The cryoscopic coefficient could be measured only for the boric acid solution of magnesium hexaborate. The remaining hexaborates are too sparingly soluble for any sort of satisfactory freezing point depression to be obtained. The cryoscopic coefficient of the boric acid solution of magnesium hexaborate varies from 1.84 to 1.88 at concentrations of 0.047-0.020. Magnesium sulfate behaves similarly at the same concentrations (Table 6).

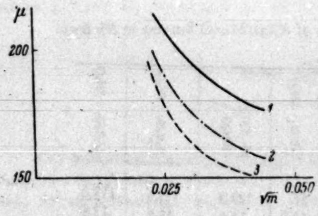

Fig. 2. The variation with dilution of the electrical conductivity of aqueous solutions of the alkaline earth diborates.

1 — $BaB_2O_4 \cdot 4H_2O$, 2 — $CaB_2O_4 \cdot 6H_2O$, 3 — $SrB_2O_4 \cdot 4H_2O$.

From this it follows that the ionic conductivity of the borate anion obtained for the boric acid solution of magnesium hexaborate and others is the ionic conductivity of the hexaborate ion. The hexaborates of the alkaline earth metals and magnesium are stable only in boric acid solution, and undergo hydrolysis in aqueous solution. It is interesting to note that in 3% boric acid the electrical conductivity of the diborates of the alkaline earth metals and magnesium also changes. The graphs of the relationship between μ_v and $\sqrt{m}$ in this case are straight lines; the ionic conductance of the borate anion has the mean value 13 $ohm^{-1} \cdot cm^2$ (Figure 1, Table 7). It is close to the ionic conductance of the hexaborate ion.

From the data in Table 7 it may be assumed that the diborates of the alkaline earth metals are converted in boric acid solution to the corresponding hexaborates:

$$2BO_2^- + 4H_3BO_3 \rightleftharpoons B_6O_{10}^{2-} + 6H_2O.$$

3. The borates of the heavy metals. The majority of the heavy metal borates containing water of crystallization do not occur naturally. They are prepared synthetically [18-26].

TABLE 5

The Cryoscopic Coefficients of the Diborates of Alkaline Earth Metals in Aqueous Solution

$CaB_2O_4 \cdot 6H_2O$		$BaB_2O_4 \cdot 4H_2O$	
m	*i*	*m*	*i*
0.010	4.38	0.010	4.15
0.008	4.32	0.008	4.38
0.006	4.73	0.006	5.57

TABLE 6

The Cryoscopic Coefficients of $MgB_6O_{10} \cdot 7.5\ H_2O$ and $MgSO_4 \cdot 7\ H_2O$ in Solution in 2% H_3BO_3

$MgB_6O_{10} \cdot 7.5H_2O$		$MgSO_4 \cdot 7H_2O$	
m	*i*	*m*	*i*
0.047	1.84	0.116	1.34
0.031	1.95	0.067	1.55
0.021	1.88	0.035	1.88

TABLE 7

The Ionic Conductance of the Anions of Alkaline Earth Metal Borates

	In aqueous solution			In 3% boric acid solution						
	$MgB_6O_{10} \cdot 7.5H_2O$	$SrB_6O_{10} \cdot 5H_2O$	$CaB_6O_{10} \cdot 5H_2O$	$MgB_6O_{10} \cdot 7.5H_2O$	$SrB_6O_{10} \cdot 5H_2O$	$CaB_6O_{10} \cdot 5H_2O$	$MgB_2O_4 \cdot 3H_2O$	$CaB_2O_4 \cdot 6H_2O$	$SrB_2O_4 \cdot 4H_2O$	$BaB_2O_4 \cdot 4H_2O$
μ_∞	173	187	187	132	136.5	139.5	134	147	148	153.5
v_∞	33.5	34.5	34	13	9.5	10.5	13.9	14.0	14.5	13.1

The heavy metal borates have as yet been insufficiently studied, since in working with them difficulties are encountered both in carrying out experiments and in evaluating the results. The reasons are to be found in the low solubility of the majority of the heavy metal borates and in the absence of the uniformity which is found in the borates of the alkali and alkaline earth metals [10, 11], since the heavy metals lie in different groups of the periodic system and form bases of different strengths, which also determines the course of the hydrolysis of their borates in aqueous solution [27].

The tetraborates of cadmium, manganese and silver in 3% boric acid solution have an ionic conductance for the anion of 16.2 $ohm^{-1} \cdot cm^2$. The same value for the ionic conductance of the anion is found for the hexaborates of cobalt and manganese in 3% boric acid solution (Table 8). This indicates that the boric acid combines with the tetraborates of the heavy metals. In this process the hexaborate ion is evidently formed, but the extent to which the conversion takes place is different for each case and depends on the concentration of the boric acid and on the nature of the anion. The combination of the boric acid with manganese tetraborate is also indicated by the lowering of the cryoscopic coefficient below unity in a solution of manganese tetraborate in 2% boric acid.

The majority of heavy metal borates undergo hydrolysis in 2% boric acid solution (Table 9). The degree of hydrolysis, however, varies in each case. Thus the nickel hexaborate $NiB_6O_{10} \cdot 10H_2O$ dissociates like a binary electrolyte: $NiB_6O_{10} \rightleftharpoons Ni^{2+} + B_6O_{10}^{2-}$.

The cryoscopic coefficient changes from 2.32 to 1.5. Cobalt hexaborate and nickel hexaborate octahydrate, on the contrary, are completely hydrolysed to the hydroxide and the free acid (i changes from 7 to 9.75). Manganese hexaborate in the same conditions dissociates into manganese tetraborate and boric acid (i changes from 4.65 to 4.85).

TABLE 8

The Ionic Conductance of the Anions of Heavy Metal Borates in 3% Boric Acid Solution

	$CdB_4O_7 \cdot 5H_2O$	$Ag_2B_4O_7 \cdot 2.5H_2O$	$MnB_4O_7 \cdot 9H_2O$	$CoB_6O_{10} \cdot 8H_2O$	$MnB_6O_{10} \cdot 8H_2O$
μ_∞	140.4	156	136	134	136
v_∞	16.4	16.0	16.6	16.8	16.6

TABLE 9

The Cryoscopic Coefficients of Heavy Metal Hexaborates in 2% Boric Acid Solution

$NiB_6O_{10} \cdot 10H_2O$		$NiB_6O_{10} \cdot 8H_2O$		$MnB_6O_{10} \cdot 8H_2O$	
m	i	m	i	m	i
0.029	2.32	0.022	6.95	0.031	4.65
0.020	2.29	0.015	7.13	0.021	4.72
0.015	2.10	0.010	8.55	0.014	4.80
0.010	2.07	0.008	9.75	0.009	4.89
0.007	1.50				

SUMMARY

1. A study has been made of the electrical conductivity and freezing point depression of dilute solutions of borates in water and in 3% boric acid in order to determine the composition of the borates in aqueous solution.

2. The stable ion in aqueous solutions of alkali metal borates is the monoborate ion, which on the addition of boric acid is capable of being converted into a polyborate ion which is evidently the pentaborate ion.

3. The stable ion in solutions of the alkaline earth borates in 3% boric acid is the hexaborate ion. The latter dissociates in aqueous solution with the separation of boric acid. The alkali metal monoborates break down in dilute aqueous solution to the corresponding hydroxide and boric acid.

4. The heavy metal borates show varying stability in 2% boric acid solution, while in 3% boric acid solution only the hexaborate ion is apparently stable.

LITERATURE CITED

[1] A. Rosenheim, F. Leyser, Z. anorg u. allgem. Chem. 119, 1 (1921).

[2] H. Menzel, Z. anorg. u. allgem. Chem. 164, 22 (1927).

[3] G. Carpeni and P. Souchay, J. chim. phys. 42, 159 (1945).

[4] G. Carpeni, Bull. Soc. Chim. 1949, 344.

[5] G. Carpeni, Bull. Soc. Chim. 1948, 628.

[6] G. Carpeni, Bull. Soc. Chim. 1947, 484.

[7] G. Carpeni, Compt.rend. 239, 1500 (1954).

[8] A. Auger, Compt. rend. 180, 1602 (1925).

[9] P. Souchay, Bull. Soc. Chim. 1953, 395.

[10] P. Souchay, Bull. Soc. Chim. 1951, 933.

[11] P. Souchay and M. Teyssedre, Compt. rend. 236, 1965 (1953).

[12] A. D. Keshan, S. G. Vimba and E. M. Schwartz, Bull. Acad. Sci. Latvian SSR 1955 No. 7, 127.

[13] H. Lunden, J. chim. phys. 5, 577 (1907).

[14] I. V. Grebenshchikov and T. A. Favorskaya, J. Russ. Phys. Chem. Soc. 61, 561 (1929).

[15] A. D. Keshan, E. M. Schwartz and S. G. Vimba, Bull. Acad. Sci. Latvian SSR 1955 No. 8, 12.

[16] A. D. Keshan and E. M. Schwatrz, Bull. Acad. Sci. Latvian SSR 1953, No. 8, 124.

[17] A. D. Keshan, Bull. Acad. Sci. Latvian SSR 1947 No. 4, 83.

[18] A. Keshan, L. Garsha and S. Vimba, Bull. Acad. Sci. Latvian SSR 1952, No. 5, 65.

[19] A. D. Keshan and K. L. Shtrenk, Bull. Acad. Sci. Latvian SSR 1953, No. 5, 92.

[20] A.D. Keshan and Ya. Mezharaups, Bull. Acad. Sci. Latvian SSR 1955, No. 7, 137.

[21] L. P. Krymova, Thesis* (Riga 1952).

[22] A. Keshan, S. Paegle and S. Vimba, Bull. Acad. Sci. Latvian SSR 1951, No. 6, 956.

[23] A. Keshan and S. Vimba, Bull. Acad. Sci. Latvian SSR 1952, No. 3, 124.

[24] S. Vimba, Thesis* (Riga 1954).

[25] A. Keshan and S. Vimba, Bull. Acad. Sci. Latvian SSR 1954, No. 3, 115.

[26] V. L. Heifets, A. L. Rotinyan, E. S. Kozich and E. N. Kalnina, J. Gen. Chem. 24, 1486 (1954) (T.p. 1471)**

[27] A. Keshan, S. Vimba and E. Schwartz, Bull. Acad. Sci. Latvian SSR 1955, No. 12, 125.

[28] Edwards and Morison, J. Am. Chem. Soc. 77, 266 (1955).

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Academy of Sciences, Institute of Chemistry, Latvian SSR

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THE PROPERTIES OF ACIDS AND BASES IN ACID SOLVENTS

X. ACID-BASE TITRATION IN MIXTURES OF ACETIC AND FORMIC ACIDS THE INFLUENCE OF THE PERMITTIVITY OF THE SOLVENT ON THE STRENGTH OF ACIDS

A. M. Shkodin, L. I. Karkuzaki and M. T. Khimenko

In recent years acid solvents have found ever widening application in analytical chemistry. The use of acid solvents as media has greatly broadened the possibilities of acid-base titration, titration of salts by displacement and the differential determination of acids and bases. It has been shown that a very great number of natural and synthetic materials, which in water are very weak bases, may be quantitatively determined by direct acid titration using acid solvents as a medium. Only in acid solvents has it proved possible to carry out the differential titration of the strongest mineral acids of equal strength (in water) in their mixtures; it is also possible to achieve the separate titration of mineral acids in a mixture with strong organic acids even in the most unfavourable concentration ratios.

A very large number of works are concerned with acetic acid. Formic acid has been less studied as a titration medium. The studies which have been carried out [1-4], however, show that formic acid is quite suitable for acid-base titration. Although the ionic product of formic acid is large (pK = 6.3), and consequently its pH scale is 6 units shorter than the pH scale of acetic acid, formic acid has a high permittivity and consequently a greater solvent power than acetic acid; it is a more acidic solvent than acetic acid and it is therefore possible to titrate in it very weak bases (urea, theobromine), whose pK in water is equal to 13-14; it is impossible to titrate them in acetic acid. Finally, acids and bases are considerably stronger in formic acid than in acetic acid.

Acid-base titration in mixtures of formic and acetic acids has been studied by Tomicek and Vidner [5]. They came to the conclusion that acid-base titration in mixtures of formic and acetic acids was impossible; no inflection was observed in the potentiometric titration curve. This is an extremely strange conclusion, since in one of our works [6] it has been shown that in a mixture of formic and acetic acids (1:1) titration is quite possible and the titration conditions are better than in pure acetic acid. In this connection a more detailed study was undertaken and the results are presented here. The study of the influence of mixed solvents on the strength of acids is also of theoretical interest.

EXPERIMENTAL

Anhydrous acetic acid was prepared from glacial acetic acid by distillation from potassium permanganate; the fraction 117.5–118° was then frozen out repeatedly and again distilled in a sectional apparatus protected from atmospheric moisture. The acetic acid obtained had m.p. 16.6° and specific conductivity $2 \cdot 10^{-8}$ ohm^{-1} cm^{-1}.

The formic acid was dried with boric oxide and vacuum distilled, then dried once more with a smaller quantity of boric oxide and again vacuum distilled. The product obtained had m.p. 8.6° and specific conductivity $7 \cdot 10^{-5}$ ohm^{-1} cm^{-1}.

The acids $HClO_4$ and $CH_3C_6H_4SO_3H$ were chemically pure. M solutions of these acids were prepared by dissolving the appropriate weights of material in anhydrous acetic acid. The water which was introduced in this process was combined with the calculated quantity of acetic anhydride. 0.1M acid solutions were prepared for titration by diluting with acetic and formic acids in such a way as to give different ratios of CH_3COOH and $HCOOH$ in the solution. The base chosen for the titration was pure freshly-distilled pyridine, and a M solution of this was prepared in the appropriate mixture of acetic and formic acids. The titrations were carried out using a high resistance potentiometer of the type PPTV-1, incorporating a valve amplifier LU-2. 10 ml of solution was taken for the titrations, which were carried out from a microburet protected from atmospheric moisture.

A quinhydrone electrode was used as indicator electrode while the reference electrode was a silver chloride electrode immersed in a saturated solution of potassium chloride in acetic acid. The arrangement of the vessel is clear from Figure 1. The use of the silver chloride electrode avoided the boundary potential; in addition, this electrode is more convenient in operation than the usual calomel electrode. The set-up is thus represented by the following:

$$\mathrm{Pt}\left|\begin{array}{l}\text{acid}\\ \text{quinhydrone}\end{array}\right|\begin{array}{c}\mathrm{KCl}\\ \mathrm{HAc}\end{array}\Bigg|\,\mathrm{AgCl, Ag.}$$

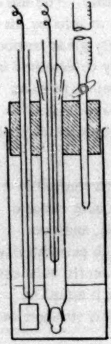

Fig. 1. Titration vessel.

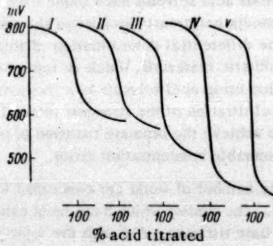

Fig. 2. Curves for the titration of perchloric acid with pyridine in mixtures of formic and acetic acids.

The titration curves are shown in Figures 2 and 3. The numbering of the curves corresponds to the numbering of the formic and acetic acid mixtures in the Table.

The potential jumps near the equivalence point (1% before and after the equivalence point) were determined from the titration curves. Their values are given in the Table, in the $(\Delta E)_{1\%}$ column. K_i/K_a — the ratio of the ionic product of the medium to the dissociation constant of the acid being titrated — characterizes the titration conditions, the dissociation constants of the acids being determined according to Roller's formula [7]:

$$E = \pm 200 \sqrt{\frac{K_i}{K_{ac}}} \sin h\, \Delta,$$

where E — previously given titration error, taken as equal to 1%, K_i — ionic product of the medium, K_a and $\underline{c}$ — the constant and concentration of the acid being titrated, sin h Δ — the hyperbolic sine of the potential jump (in mV), multiplied by 0.158.

Since the ionic product of the medium is unknown and there are no data for calculating it, we determined its value in the following manner. As we have established [8], the pK of mineral acids in acid solvents is linearly related to the permittivity of the medium. Making use of this fact, we determined pK_a for perchloric acid as the strongest acid, and found K_i –the ionic product of the medium– from Roller's formula. The values of pK_i are given in the Table. These values of K_i were used to calculate the dissociation constants of toluenesulfonic acid. It is interesting to note that the values for K_i found in this way for mixtures of formic and acetic acids are of the same order as the values calculated by the combination rule from the ionic products of formic and acetic acids, whose pK_i equal 6.3 and 12.6 respectively. It may be thought that the constants obtained in this way for perchloric and consequently for toluenesulfonic acids are relative values. In fact this is not so. The constants for perchloric acid have also been determined for certain mixtures from the electrical conductivity. These proved to be very close to the values found from the relationship between pK_a and $1/D$.

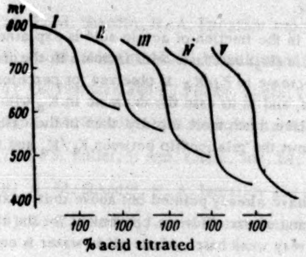

Fig. 3. Curves for the titration of toluenesulfonic acid with pyridine in mixtures of formic and acetic acids.

The permittivity of the mixtures was calculated by us from the combination rule:

$$D = \frac{v_1 D_1 + v_2 D_2}{v_1 + v_2},$$

where D_1 and D_2 – the permittivities of formic acid ($D_1 = 57$) and acetic acid ($D_2 = 6.2$), v_1 and v_2 – percentage content of the components of the mixture.

This rule should and in fact does apply, with some approximation, to mixtures of solvents of the same character. Thus, for example, the values of the permittivity of mixtures of methyl and ethyl alcohol with water, calculated by us according to the combination rule, proved to be in a good agreement with the experimental values given in the literature [9].

TABLE

Specimen No.	Composition of solvent (mole %)		D	pK_i	$HClO_4$, $c = 0{,}1$			$CH_3C_6H_4SO_3H$, $c = 0.078$			ΔpK_a
	$HCOOH$	CH_3COOH			$(\Delta E)_{\eta\%}$ (mV)	$-\log\frac{K_i}{K_a}$	pK_a	$(\Delta E)_{\eta\%}$ (mV)	$-\log\frac{K_i}{K_a}$	pK_a	
I	78	22	41.7	6.4	7.5	5.9	0.6	3.0	5.1	1.3	0.7
II	60	40	31.5	7.2	10.0	6.3	0.8	4.7	5.5	1.7	0.9
III	33	67	18.7	9.3	20.0	7.7	1.6	7.0	6.0	3.3	1.7
IV	14	86	11.1	11.4	24	8.4	3.0	9.2	6.3	5.2	2.2
V	7	93	8.5	12.1	40	9.0	4.0	9.4	6.3	6.6	2.6

DISCUSSION OF RESULTS

The potentiometric titration curves show clearly that acid-base titration is quite possible in mixtures of formic and acetic acids. In all cases the inflections in the curve are clearly defined; moreover, the greater the mole fraction of acetic acid, the greater the potential jump. There is consequently no justification for the conclusion reached by Tomicek and Vidner that mixtures of formic and acetic acids are unsuitable as media for acid-base titration. The reason for the lack of success in these authors' experiments was apparently the fact that they added a large amount of acetic anhydride straight away to the formic acid. This brought about the decomposition of the latter with the formation of water.

The improvement in the titration conditions with increase in the fraction of acetic acid is explained by the decrease in the ratio K_i/K_a. Although the constant of the acid (K_a) decreases with increase in the fraction of acetic acid, K_i decreases more rapidly than K_a. A greater decrease in K_i/K_a is observed for perchloric acid than for toluenesulfonic acid. The latter is the weaker acid, and in its case the decrease in K_a with increase in the acetic acid fraction in the mixed solvent takes place much more rapidly than in the case of perchloric acid. This is clearly illustrated in Figure 4, which shows the relationship between K_i/K_a and the composition of the mixture.

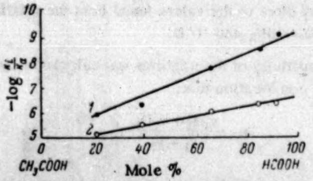

Fig. 4. Relationship between K_i/K_a and the composition of the solvent. 1) perchloric acid, 2) toluenesulfonic acid.

We have already pointed out above that mixtures of formic and acetic acids are convenient for the titration of very weak bases, whose pK in water is equal to 13 and above (urea, theobromine etc.). The presence of the formic acid ensures a sufficiently high solubility of the base, while the presence of the acetic acid in the solvent decreases its ionic product, which increases the accuracy of the titration.

The study of the influence of mixed solvents of acid character on the strength of acids is also of theoretical interest. As is known, the differentiating action of glacial acetic acid on the strength of mineral acids was explained by Hantzsch by the acidity of the solvent. Our studies have shown [2-4,8], however, that mineral acids remain strong in formic acid and are not differentiated, although formic acid is a more acidic solvent than acetic acid. The strength of the acids and the differentiating action is related to the permittivity of the acid solvents, although the basicity of the solvent has also some significance.

In the study of the influence of permittivity, mixtures with dioxane or other "neutral" solvents with low dielectric constant are usually employed. We chose mixtures of formic and acetic acids, i.e. solvents of the same character but with markedly different dielectric properties.

The results of the investigation show that in mixed acid solvents the strength of mineral acids is related to the permittivity value. The lower the latter, the weaker the acid. And the lower the permittivity, the greater is the differentiating action of the mixed acid solvents. This is illustrated by the value of ΔpK, i.e. the difference between pK for perchloric acid and pK for toluenesulfonic acid in the same solvent.

SUMMARY

1. A study has been made of the influence of mixtures of formic and acetic acids of different composition on the strength of mineral acids.

2. It has been shown that mixtures of formic and acetic acids are quite suitable as media for acid-base titration. The relationship between the titration conditions and the composition of the mixture has been examined, and the ratios of the ionic product of the medium to the constant of the acid, which characterize the titration conditions, have been calculated.

3. It has been established that with increase in the mole fraction of the acetic acid, i.e. with decrease in the permittivity of the mixture, the strength of mineral acids decreases. The differentiating action increases with decrease in the permittivity of the mixed solvents.

LITERATURE CITED

[1] L. P. Hammett and N. Dietz, J. Am. Chem. Soc. 52, 4795 (1930).

[2] A. M. Shkodin, N. A. Izmailov and N. P. Dzyuba, J. Gen. Chem. 20, 1999 (1950) (T.p.2071) *

[3] A. M. Shkodin, N. A. Izmailov and N. P. Dzyuba, J. Anal. Chem. 6, 273 (1951).

[4] A. M. Shkodin, M. A. Izmailov and N. P. Dzyuba, J. Gen. Chem. 23, 27 (1953) (T.p. 25)*

[5] O. Tomicek and P. Vidner, Chem. Listy 47, 521 (1953); Russ. J. Chem (1953), 341 .

[6] A. M. Shkodin, L. I. Karkuzaki and Z. S. Dybskaya, Trans Inst. Chem. Kharkov Univ. 14,33 (1956).

[7] P. S. Roller, J. Am. Chem. Soc. 54, 3485 (1932).

[8] A. M. Shkodin, N. A. Izmailov and N. P. Dzyuba, Ukrain. Chem. J. 20, 595 (1954).

[9] G. C. Akerlof, J. Am. Chem. Soc. 54, 4125 (1932).

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Kharkov State University

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* T.p. = C.B. Translation pagination.

CERTAIN PROPERTIES OF SUPERSATURATED SOLUTIONS OF Na_2SO_4 AND ITS CRYSTALLINE HYDRATES

Khr. Balarev

The present work is devoted to the question of spontaneous crystallization of supersaturated solutions and in particular of Na_2SO_4 solutions, and also to a determination of the rate of the spontaneous process

$$10\ Na_2SO_4 \cdot 7H_2O = 7Na_2SO_4 \cdot 10H_2O + 3Na_2SO_4 \qquad (A)$$

Not all supersaturated solutions crystallize when the sides of the vessel are rubbed with a glass rod. Thus, for example, NaBr solutions crystallize as soon as the glass rod touches the walls, whereas solutions of Na_2SO_4 and $NaOOCH_3$ do not possess this property [1]. The experiments carried out have shown that the properties mentioned do not change down to temperatures of −4° at concentrations from 18 to 31% by weight.

The explanation given for the fact that supersaturated solutions crystallize when the vessel is rubbed with a glass rod, namely, that tiny particles are broken off and function as nuclei, has been rejected on the basis of the following experiments which have been carried out.

Pieces of different glass were placed in an agate mortar to which a saturated solution of Na_2SO_4 was added, and the pieces ground up. This did not lead to crystallization. Supersaturated solutions of Na_2SO_4 again did not crystallize when the minerals fluorite, gypsum or calcite were ground up in them. In contrast to this, supersaturated solutions of NaBr crystallize even when the rubbing is carried out with a glass rod tipped with rubber.

Every supersaturated solution has its own rate of spontaneous crystallization, which is measured by the number of nuclei appearing spontaneously in unit volume of the solution in unit time at a given supersaturation. Experiments carried out with different initial-solution concentrations have shown that supersaturated solutions of Na_2SO_4 can stand for months in dishes covered with clock glasses without giving any precipitate of $Na_2SO_4 \cdot 10H_2O$ crystals, which shows that the rate of spontaneous crystallization of this crystal hydrate is low. In all cases $Na_2SO_4 \cdot 7H_2O$ was formed.* Thus, independently of evaporation of the solvent, the concentration corresponded to that which a saturated solution of $Na_2SO_4 \cdot 7H_2O$ would have at that temperature. Supersaturated solutions of $NaOOCCH_3$ also have a low rate of spontaneous crystallization. Under similar conditions, supersaturated solutions of NaBr are stable for no more than two days. From these examples a connection has been established between the rate of spontaneous crystallization and the effect of rubbing.

It has been established that both contradictory properties of supersaturated solutions when the containing vessels are rubbed with a glass rod (the crystallization of $NaBr \cdot 2H_2O$ and the absence of crystallization in the case of $Na_2SO_4 \cdot 10H_2O$) are related to one another and explained by the existence of a transitional supersaturated solution. For example, if a solution of Na_2SO_4 (saturated at 100°) is brought to a definite temperature, say 12°, and then cooled comparatively rapidly to 8.5°, without rubbing, then in many cases $Na_2SO_4 \cdot 7H_2O$ crystallizes spontaneously; solutions which do not crystallize, however, are also found (see Table). If such a solution, which has not crystallized, and which has been kept for, say, one day at that definite temperature (8.5°), is subjected to friction, or if the same solution is subjected to friction without the rapid cooling, then no crystallization takes place in either case.

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* The crystal hydrate $Na_2SO_4 \cdot 7H_2O$ is metastable, as a result of which it has a higher solubility at the given temperature.

TABLE

No. of experiment	Time (in hours)	Temp (±0.2°)	Number of initial solutions	Concentration (% by weight)	Number of solutions crystallized
1	0	12°	4	29.8	—
	24	12	4		0
	31	12	4		0
	44	8.5	4		3
	52	8.5	1		0
2	0	12	4	29.8	—
	10	12	4		0
	20	8.5	4		2
	28	8.5	2		0
3	8	16	8	29.8	0
	23	13	8		3
	31	13	5		0
4	0	13	6	29.8	—
	168	13	6		0
	180	5.5	6		6

Experiments 1 and 2 were carried out simultaneously, but the solutions in experiment 2 were prepared and brought to the constant temperature 24 hours afer the solutions in experiment 1 were prepared.

The friction in our experiments was achieved using a stirrer with centrifugal attachment (a) shown in the Figure, and the time of rubbing did not exceed 1 hour. In the case of Na_2SO_4, when cooling was accompained by friction, the heptahydrated sulfate always crystallized out.

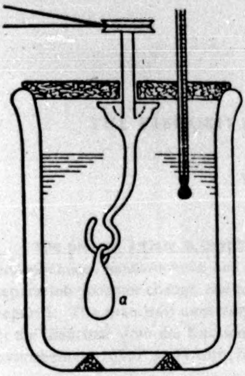
The rate of spontaneous crystallization of $Na_2SO_4 \cdot 7H_2O$, although very much greater than the rate of crystallization of $Na_2SO_4 \cdot 10H_2O$, is nevertheless low, and is considerably increased only by rapid lowering of the temperature. Thus in this case a simple connection is established between the rate of spontaneous crystallization and the friction effect.

If the same supersaturated solution, under identical conditions, can have different rates of spontaneous crystallization depending on the preliminary treatment, then this must be caused by different structures in the solutions. Ageing, i.e. the change in the properties of a rapidly cooled solution with time, is probably related to the rate of formation of different quasicrystalline groupings under the given conditions, which has an influence on the probability of formation of an actual crystalline nucleus.

The facts described below indicate that a thin layer (adsorbed) of a crystalline salt on glass, metal or charcoal has a comparatively low rate of dissolution. Thus if the glass rod used for rubbing the sides of the vessel is previously kept in contact (for several minutes) with $Na_2SO_4 \cdot 10H_2O$ crystals and is not very carefully washed in running water (for example 1-2 minutes with the rod moving vigorously) and after this in cold distilled water, then when this rod is immersed in a supersaturated solution no crystallization takes place for a certain time (for example up to half an hour and in rare instances up to 1 hour) after which the solution begins to crystallize from the point of contact of the rod with the crystalline phase, i.e. from the above-mentioned adsorbed layer. When rubbing takes place with such a rod, however, crystallization takes place at once. Similar experiments were carried out with $NaOOCCH_3 \cdot 3H_2O$ and $Na_2SO_4 \cdot 7H_2O$ instead of $Na_2SO_4 \cdot 10H_2O$ with the same result. If the rod is washed for a long time in running water (for example for several hours) then in the majority of cases no amount of rubbing brought about crystallization. The same effect is found if the dish is subjected to the same treatment. For the case described the nature of the glass used plays some part. Thus, for example, no effect of this sort is observed at all with quartz glass, while in the case of Jena glass the effect is observed under those conditions where the contact with the crystals and the washing with water takes place so that the temperature of the system does not exceed 7° and at 15° the effect is again not observed. Bohemian glass gives a positive effect up to 20°.

Experiments were carried out with metallic rods—copper, iron and nickel—as well as with glass rods. When these rods, after being in contact with the crystalline phase and left for several days in cold running water, were rubbed against the sides of a vessel with a saturated solution, $Na_2SO_4 \cdot 10H_2O$ crystallized immediately. A particularly powerful effect was brought about by a carbon rod. When this had been washed for a long time in running water (10 days) and immersed in a solution, it did not bring about crystallization, which began only on rubbing. If the carbon rod is left in the supersaturated solution without rubbing, then the solution may not crystallize even after 2 days. The carbon rod retains the property of being able to bring about crystallization even up to 27°, but a short immersion in water (for several seconds) at temperatures above 30° is sufficient to rob it of this property.

An explanation of this phenomenon can be given only if we assume that the fine crystals, in contact with definite surfaces, change their properties, and in particular, the property of bringing supersaturated solutions out of their metastable state. The existence of such crystalline layers has been established by other authors.



In this respect considerable interest is attached to a work [2] whose results agree fully with the data from our work. In a paper by Richards [3], similar observations are taken as the basis for postulating the existence of crystalline forms melting at higher temperatures than the melting point of the crystalline mass. Particularly extensive studies have been made in this connection by V. I. Danilov [4], who has worked with aqueous solutions of salts and with melts of organic compounds and metals.

It is known that fine crystals have a measurably greater vapor pressure and correspondingly greater solubility than macrocrystals. In all the cases described above, however, the thin crystalline layer, with no free surface, probably alters the properties of the tiny crystals. The possibility that $Na_2SO_4 \cdot 7H_2O$ breaks down on being rubbed was examined. To this end, supersaturated solutions were left to stand in dishes covered with clock glasses for a period of 8 months while the room temperature varied* within the range 6-25°, no particular precautions being taken against convection. Crystals of $Na_2SO_4 \cdot 7H_2O$ separated on the bottom of the dish, while creeping crystals of composition $Na_2SO_4 \cdot 7H_2O$ were formed on the sides. No decahydrated sodium sulfate crystallized when the bottom or the walls were rubbed. The solutions were, however, supersaturated with this material, since on the introduction of a seed, crystallization began.

When crystals of any crystal hydrate are rubbed, then, as is well known, efflorescence, i.e. the formation of a new phase, begins from the damaged spot. By analogy it may be expected that damaged crystals of $Na_2SO_4 \cdot 7H_2O$ in the case described may also be converted spontaneously into new crystalline phases according to the equation (A). This, however, does not take place.

LITERATURE CITED

[1] D. Balarew, Kolloid-Z. 101, 50 (1942).

[2] S. Roginsky, L. Sena and Ya. B. Zeldovich, J. Phys. Chem. 1, 630 (1932).

[3] W. Richards, J. Am. Chem. Soc. 54, 479 (1932).

[4] V. I. Danilov, J. Exp. Theoret. Phys. 18, 886 (1948); 19, 908 (1949); V. I. Danilov and V. E. Neimark, J. Exp. Theoret. Phys. 10, 942 (1940).

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Institute of Inorganic Chemistry, Sofia

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* The experiments were carried out in a thermostat. After the supersaturated solutions of Na_2SO_4 had stood for more than 4 months at 25°, no $Na_2SO_4 \cdot 10H_2O$ had crystallized, but as a result of evaporation and concentration of the solution the anhydrous salt crystallized out. The solution above these crystals proved to be supersaturated with $Na_2SO_4 \cdot 10H_2O$.

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When [illegible] of a new phase [illegible] to the equation (4) [illegible]

(1) D. Balarew, [illegible]

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THE VISCOSITY OF BINARY SYSTEMS WITH CHLORAL. IV.

V. V. Udovenko and R. I. Khomenko

The present article is devoted to a study of the viscosity of binary systems of chloral with acetophenone, benzophenone, benzaldehyde and salicylaldehyde. In these systems the viscosity of the mixtures after their preparation does not change and so the measurements were carried out immediately after the mixtures were prepared. The materials necessary for the investigation were previously purified by repeated distillation and for the practical work the fractions with the following boiling points were taken: acetophenone 80.0° at 12 mm, benzophenone 161.0° at 11 mm, benzaldehyde 177.2° at 731 mm and salicylaldehyde 193.0° at 727 mm.

The measurement of viscosity and density in the system chloral–acetophenone was carried out at 25, 50 and 75°. The results of the measurements are given in Table 1. The viscosity isotherms at all temperatures have the form of straight lines, while the density isotherms are slightly convex towards the composition axis.

TABLE 1

The System Chloral–Acetophenone

Chloral content (mole %)	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	1.6369	1.0920	0.7983	1.0246	1.0035	0.9823
9.86	1.5918	1.0770	0.7923	1.0633	1.0415	1.0195
19.81	1.5319	1.0456	0.7735	1.1054	1.0805	1.0586
30.04	1.4761	1.0128	0.7544	1.1489	1.1242	1.0975
40.67	1.4115	0.9845	0.7330	1.1967	1.1691	1.1437
49.91	1.3578	0.9509	0.7111	1.2406	1.2117	1.1840
59.69	1.2919	0.9060	0.6922	1.2899	1.2587	1.2284
69.97	1.2366	0.8759	0.6690	1.3126	1.3098	1.2785
80.03	1.1509	0.8355	0.6453	1.3922	1.3560	1.3192
89.75	1.0962	0.7944	0.6048	1.4540	1.4138	1.3756
100.00	1.0552	0.7641	0.5885	1.5013	1.4603	1.4186

In the system chloral–benzophenone the viscosity and density were measured at 25, 50 and 75°. The results of the measurements are given in Table 2. The viscosity and density isotherms at all temperatures are convex towards the composition axis.

In the system chloral–benzaldehyde the viscosity and density were similarly measured at 25, 50 and 75°, but in contrast to the previous two systems the measurements were begun several hours after the mixtures were prepared since a slight change in the viscosity at first takes place. The results of the measurement of the viscosity and density are given in Table 3. The viscosity isotherms are curves concave towards the composition axis, while the density isotherms are straight lines.

TABLE 2

The System Chloral–Benzophenone

Chloral content (mole %)	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	14.666	5.2934	2.7537	1.1068	1.0799	1.0552
9.95	11.730	4.6384	2.5161	1.1239	1.1069	1.0865
19.95	8.7865	3.8736	2.2128	1.1555	1.1338	1.1124
28.65	7.0611	3.3207	1.9721	1.1830	1.1596	1.1334
40.10	5.2269	2.6853	1.6702	1.2190	1.1938	1.1601
49.86	3.9703	2.2005	1.4444	1.2610	1.2350	1.2101
58.49	3.1629	1.8586	1.2630	1.2964	1.2678	1.2399
69.90	2.3802	1.4842	1.0460	1.3417	1.3116	1.2821
79.39	1.8607	1.2272	0.8892	1.3845	1.3529	1.3205
88.87	1.4302	0.9867	0.7329	1.4347	1.4010	1.3544
100.00	1.0552	0.7641	0.5885	1.5013	1.4603	1.4186

TABLE 3

The System Chloral–Benzaldehyde

Chloral content (mole %)	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	1.3870	0.9745	0.7369	1.0455	1.0234	1.0001
11.28	1.3843	0.9713	0.7366	1.0959	1.0707	1.0481
21.15	1.3660	0.9495	0.7219	1.1400	1.1153	1.0895
30.13	1.3551	0.9475	0.7192	1.1830	1.1530	1.1277
39.93	1.3302	0.9395	0.7039	1.2258	1.1995	1.1689
49.85	1.3051	0.9009	0.6890	1.2735	1.2435	1.2127
64.83	1.2509	0.8728	0.6718	1.3464	1.3112	1.2765
80.01	1.1548	0.8150	0.6297	1.4101	1.3746	1.3382
90.29	1.1196	0.7984	0.6115	1.4645	1.4248	1.3860
100.00	1.0552	0.7641	0.5885	1.5013	1.4603	1.4186

The measurement of the viscosity and density in the system chloral–salicylaldehyde were carried out at 25, 50 and 75°. The results of the measurements are given in Table 4. The viscosity isotherms are slightly convex towards the composition axis while those of the density are straight lines.

When the results of the study of the viscosity in the system chloral–acetophenone are examined, only an extremely slight reaction between the components can be observed, as shown by the linear character of the viscosity isotherm. It is known from the literature that chloral reacts with acetophenone in the presence of acetic acid as catalyst with the formation of the crystalline compound chloralacetophenone $CCl_3CHOHCH_2COC_6H_5$ [1]. Our measurements show that in the given conditions, chloral and acetophenone do not form such a compound by direct reaction. There is similarly no reaction in the system chloral–benzophenone.

In the system chloral–benzaldehyde, the viscosity isotherms are concave towards the composition axis, which provides evidence that reaction has taken place. This reaction is, however, weakly defined and contrasts strongly with that which is observed in systems with alcohols [2,3]. Judging from the viscosity diagram, a dipole interaction is probably taking place in the chloral–benzaldehyde system.

TABLE 4

The system chloral–salicylaldehyde

Chloral content (mole %)	Viscosity			Density		
	25°	50°	75°	25°	50°	75°
0.00	2.5012	1.5361	1.0630	1.1603	1.1380	1.1130
9.98	2.3121	1.4457	1.0171	1.1930	1.1673	1.1427
19.04	2.0972	1.3371	0.9595	1.2249	1.1914	1.1717
29.91	1.9165	1.2602	0.9093	1.2646	1.2372	1.2086
40.08	1.7497	1.1679	0.8643	1.2977	1.2679	1.2406
51.65	1.5807	1.0815	0.7993	1.3401	1.3083	1.2781
64.09	1.4244	0.9822	0.7387	1.3753	1.3443	1.3109
75.91	1.2870	0.9032	0.6840	1.4188	1.3826	1.3471
89.63	1.1185	0.7963	0.6145	1.4655	1.4290	1.3929
100.00	1.0552	0.7641	0.5885	1.5013	1.4603	1.4186

From the viscosity diagrams in the system chloral–salicylaldehyde, no reaction takes place between the components, in spite of the fact that salicylaldehyde has a hydroxyl group in the molecule. As optical studies have shown [4], the spectrum of salicylaldehyde does not show the absorption bands characteristic of the hydroxyl group, since the hydrogen of the hydroxyl group forms an intramolecular hydrogen bond with the oxygen of the carbonyl group situated in the ortho-position [5]. Since the formation of an intramolecular hydrogen bond alters sharply the physicochemical properties of a substance, this also explains the absence of reaction between chloral and salicylaldehyde.

SUMMARY

1. A study has been made of the viscosity and density of the systems: chloral– acetophenone, chloral–benzophenone, chloral–benzaldehyde and chloral–salicylaldehyde at 25, 50 and 75°.

2. It has been established that in the systems studied there is no clearly defined reaction between the components leading to the formation of a definite chemical compound.

LITERATURE CITED

[1] W. Koenigs, Ber. 25, 793 (1892).

[2] N. S. Kurnakov and N. N. Efremov, J. Russ. Chem. Soc. 45, 329 (1913).

[3] V. V. Udovenko, E. I. Kalabanovskaya and M. F. Prokopyeva, J. Gen. Chem. 19, 165 (1949) (T.p.149)*

[4] M. I. Batuev, J. Phys. Chem. 14, 1064 (1940).

[5] M. I. Batuev, Prog. Chem. 10, 416 (1941)

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a compound by direct reaction. There is similarly no [illegible] in the [illegible]

In the system chloral–benzaldehyde, the viscosity isotherms [illegible] toward the [illegible] which provides evidence that [illegible] strongly with that which is observed in systems with [illegible]

TABLE 4

The system chloral–salicylaldehyde

Chloral content (mole %)	Viscosity			Density		
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
100.00	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

interaction is probably taking place in the chloral–benzaldehyde system.

From the viscosity isotherms in the system chloral–salicylaldehyde, [illegible] between the components, in spite of the fact that salicylaldehyde has a hydroxyl group in the molecule. As other workers have shown [4], the unassociated salicylaldehyde does not have the [illegible] characteristic of the hydroxyl group, since the hydrogen of the hydroxyl group forms an intramolecular hydrogen bond with the oxygen of the carbonyl group situated in the ortho position [5]. Since the formation of an intramolecular hydrogen bond alters sharply the physicochemical [illegible] this also explains the absence of interaction between chloral and salicylaldehyde [3].

1. A study has been made of the viscosity and density of the systems: chloral–[illegible], chloral–benzophenone, chloral–benzaldehyde, and chloral–salicylaldehyde.

2. It has been established that in the systems studied there is no chemical interaction between the components leading to the formation of a definite chemical compound.

LITERATURE CITED

[1] W. Koenigs, Ber. 25, [illegible] (1892).

[2] M. S. [illegible]

[3] V. V. Udovenko, [illegible] J. Gen. Chem. [illegible] (T.p. [illegible])*

[4] M. L. [illegible] J. Phys. Chem. [illegible]

[5] M. T. [illegible]

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THE APPLICATION OF CHROMATOGRAPHY TO THE STUDY OF THE REACTIONS OF DIMETHYLGLYOXIME WITH METAL CATIONS. I.

A. M. Gurvich

Dimethylglyoxime (in future referred to as H_2Dm [1]) combines with the cations of such metals as Ni, Co, Fe and Cu to form compounds of varied composition and structure (see, for example, [2-10]), for the study of whose properties the classical preparative method, which makes it possible to isolate and analyse only those compounds which are the most stable in the given conditions and are difficultly soluble, proves insufficient. Attention has therefore been concentrated in recent years on physico-chemical methods of investigation, and on spectrophotometric methods in particular [7-10]. The problems being tackled can only be more or less fully solved, however, by the collective application of a number of independent methods of investigation. The working out and application of new methods of investigating the reactions of complex formation are therefore among the most essential requirements in the field of the chemistry of complex compounds [11]. The study of the reactions of H_2Dm with cations is also of interest from the point of view of applied chemistry as a result of the ever-widening application of dimethylglyoxime in analytical and preparative chemistry [5,6,12].

We have worked out, and applied to the study of the reactions with cations, the following method, which is a variation of the chromatographic method of M. S. Tsvet. As is known [13], H_2Dm, in its reaction with metal cations, may either form coordinate bonds only, or, together with them, form bonds with the main valencies, splitting off the hydrogen ion H+ in the process.

In those cases where a sparingly soluble compound is formed, for example, $Ni(HDm)_2$, the acid which is formed in the reaction process may be easily separated from the precipitate of the inner complex salt and titrated [14]. To separate the acid from soluble complex compounds we have used a chromatographic method based on the difference in the nature of the adsorption of nonelectrolytes and strong electrolytes by active carbon. It is known that a strong mineral acid adsorbed from aqueous solution by carbon activated at a high temperature cannot be completely desorbed by water even at the boiling point [15]. The irreversibility of the adsorption of a strong acid by active carbon is explained by the theories of surface oxides (Schiloff, Tschmutoff [16]) and of the gas electrode (Frumkin et al. [17]) as due to the reaction of the H^+ ion with the hydroxyl groups of the electrical double layer formed on the surface of carbon immersed in water. Together with this so-called "hydrolytic" adsorption, molecular adsorption of the acids as surface-active agents also takes place [18,19]. By saturating active carbon with hydrochloric acid and washing off the molecularly adsorbed acid with water, we render the carbon practically incapable of irreversible adsorption of acid. Dimethylglyoxime is then introduced into a column of such carbon by adsorption from a saturated (0.04%) aqueous solution, while the filtration of the solution through the column is stopped before H_2Dm passes through, so that the lower part of the column consists of a layer of carbon containing no dimethylglyoxime. When this column has been washed with water, a definite quantity of a dilute (~0.025 N) solution of the salt (chloride or sulfate) of the metal reacting with the H_2Dm is introduced into it. The acid formed in this process is adsorbed by the carbon chiefly (90-98%) in the molecular form, which enables the reaction to go more fully to completion in the direction of formation of the corresponding complex compound and at the same time enables the acid to be titrated after desorption with water; in this way the number of saltforming oxime groups is determined and this in turn makes it possible to reach various conclusions on the structure of the compounds formed in the column.

For example, the formation of the following compounds may be postulated for cobalt in these conditions: $Co(HDm)_2$, $[Co(HDm)_2(H_2O)_2]Cl$ and $[Co(H_2Dm)_2]Cl_2$ [8, 10, 13]. In the case of the formation of $Co(HDm)_2$

2 moles of H^+ should be liberated for every mole of Co^{++} which combines with H_2Dm:

$$CoCl_2 + 2H_2Dm = Co(HDm)_2 + 2HCl.$$

The formation of one mole of $[Co(HDm)_2(H_2O)_2]Cl$ should be accompanied by the liberation of one mole of H^+:

$$CoCl_2 + 2H_2Dm + \frac{1}{4} O_2 + \frac{3}{2} H_2O = [Co(HDm)_2(H_2O)_2]Cl + HCl.$$

Finally, if the reaction product is $[Co(H_2Dm)_2]Cl_2$, no acid should be liberated.

For Cu^{++} in the reaction conditions of a column of the type described, which we shall refer to in future as a charcoal-dimethylglyoxime column, the formation of two compounds – $Cu(HDm)_2$ and $(CuHDm)Cl$ – may be postulated [7]. We may similarly expect the liberation of two or one moles of acid for every mole of Cu^{++} reacting with the H_2Dm. A similar situation obtains for the reaction of divalent iron with H_2Dm [9].

EXPERIMENTAL

We used carbon differing from ordinary mark "A" clarifying carbon in the size of the particles, which were 0.2-0.5 mm in diameter, and purified from ash impurities in the same way as the carbon used for the chromatographic purification of the raw material for phosphors [12]. In order to bring the chemical adsorption * to a minimum, which is determined by the kinetics of the process [20] (equilibrium in the adsorption of the acid by the carbon cannot be reached in time intervals measured in days), we treated the carbon with concentrated hydrochloric or sulfuric acid in static conditions, first with heating and then in the cold, or else by passing a dilute solution of HCl or H_2SO_4 through the column until an approximately constant acid concentration was established in the filtrate (~ 96% of the starting concentration). The molecularly adsorbed acid was then washed from the carbon. We observed that in the conditions of the dynamic experiment, in which 0.025 N HCl solution was used, the carbon adsorbed chemically 0.04-0.06 milliequivalents HCl per gram of carbon and adsorbed physically 0.14-0.16 milliequivalents/g [15].

H_2Dm was then introduced by adsorption from 750-1200 ml of an aqueous solution saturated at 18-20° into a column previously saturated with water and prepared in all experiments from 6 g of air-dry carbon. It should be noted that neither the H_2Dm nor the salts of Ni^{++}, Co^{++}, Cu^{++} and Fe^{++} displace the acid from carbon which has been treated as described above. The preparation of the column for the experiment was completed by washing with 200-300 ml water.

The experiments were carried out with the chlorides and sulfates and the column was appropriately treated beforehand with either HCl or H_2SO_4 as described above, although in work using the sulfates on columns saturated with HCl, the results obtained differed only very slightly from the results of experiments on carbon treated with H_2SO_4. In each experiment 20 ml of ~ 0.025 N solution of the Ni^{++}, Cu^{++}, Co^{++} or Fe^{++} salt was introduced on to the column, after which the column was washed with water. The filtrate was collected in 100-200 ml portions and titrated with 0.1 N NaOH using methyl orange.

The choice of volume and concentration of solution was governed by the desirability of carrying the reversible reaction as far as possible in the direction of formation of the appropriate dimethylglyoxime compound and at the same time giving the least possible reduction in the accuracy of the experiment due to the decrease in the quantity of the cation reacting with the dimethylglyoxime. No buffer mixture was added to the solution since it was desired to obtain a strong mineral acid as reaction product.

In the experiment with Cu^{++} the filtrate did not liberate iodine from KI, while a drop test for Cu^{++} with rubeanic acid gave a negative result.

The degree of adsorption of Ni^{++} and Co^{++} by the column was likewise close to 100%, but in these experiments we introduced a correction for the quantity of unreacted cation obtained by determining the total salt concentration ($NaCl + CoCl_2$ or $NaCl + NiCl_2$) in the first 300 ml of filtrate after titration, using a column of cation exchange resin in the H-form. To establish the quantity of acid in the filtrate from the experiment with divalent iron, which is adsorbed by the column to the extent of only 30-40%, we used a H-cation exchanger

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* We used here the terminology suggested by M. M. Dubinin [21].

to determine the sum of $Fe^{++} + H^{+}$ [22] and a gravimetric method to determine the Fe content. The experiment was started immediately after the preparation of the $FeSO_4$ solution. No reductant was added to the starting solution. Its role is taken in the column by the carbon [23]. The pH of the starting solution was 4.2, while the pH of the solutions of the salts of the other cations was in the range 5-6.

In all the experiments we washed the acid from the carbon until the pH of the filtrate had reached 3.8-3.9, both after treating the carbon with acid and after completing the reaction between the metal cation and the dimethylglyoxime. This required approximately 800 ml of water and led to satisfactory agreement of results in a series of successive experiments on the same column.

The experimental results (including those of a preliminary experiment carried out to determine the residual "hydrolytic" adsorption of the acid under conditions close to those of the other experiments) are given in the table.

TABLE

Cation	Solution concentration (N)	Ratio of milliequiv. of acid liberated in the filtrate to milliequiv. of cation reacting (or of acid added to the column) (%)
H^{+}	0.0250	90.8
Ni^{++}	0.0294	86.8
Cu^{++}	0.0224	86.4
Co^{++}	0.0260	95.5
Fe^{++}	0.0337	85.9

The results for each cation are the mean of at least two experiments, the carbon used in these experiments being previously treated with concentrated hydrochloric or sulfuric acid as described above. Experiments carried out with carbon treated with acid directly on the column gave results which were substantially the same as those given in the table.

DISCUSSION OF RESULTS

Examination of the data given in the table shows that when the reaction between H_2Dm and Ni^{++}, Cu^{++}, Co^{++} and Fe^{++} is carried out in the conditions obtaining in a chromatographic carbon-dimethylglyoxime column of the type described, approximately one milliequivalent of H^{+} ion is liberated for every milliequivalent of cation entering into the reaction. It is difficult to achieve a greater accuracy in these experiments, both as a result of the particular nature of the kinetics of the irreversible adsorption of acid by active carbon and also as a result of the length of time taken by the process of desorption of the molecularly adsorbed acid on the carbon. The slightly low results for Ni^{++} and Cu^{++} are explained by the fact that the reaction in these cases takes place for the most part in the upper layers of the column, as a result of which a solution of acid is formed whose concentration may considerably (according to an approximate calculation—by 5-10 times) exceed the concentration of the acid (0.0250 N) in the preliminary experiment. This brings about a more intense adsorption of the acid than in the experiment with Co^{++}, which in the given conditions apparently forms a less stable compound with H_2Dm, which is indicated by the fact that the appearance of Co^{++} in the filtrate is observed after the passage of a smaller volume of starting solution than is required for the appearance of Cu^{++} and Ni^{++}. In the case of Fe^{++}, the somewhat low result may be caused by the fact that the carbon, whose adsorptive powers towards Fe^{++} are greater than towards Co^{++} [20], may not lose completely its power to adsorb Fe^{++} hydrolytically, even after the treatment with acid. Evidence for this is provided by the experiments of Shilov and Lepin, who showed [20] that in the presence of HCl the adsorption of $CdCl_2$, which is almost identical to $CoCl_2$ in its adsorption on active carbon, is lowered to zero, whereas the adsorption of $FeSO_4$ in the presence of H_2SO_4 falls only to 13.5% of the original.

The liberation of an equivalent amount of acid in the reaction of a divalent metal cation with H_2Dm may result from the formation of a compound of the type $Me(HDm)_2$ or the type MeDm. Since, however, the second oxime group of H_2Dm functions as a salt-forming group only in alkaline medium [7,9,13], the only conclusion to be reached is that in the reaction with H_2Dm, under the conditions obtaining in a chromatographic column of the type described, all four of the cations studied—Ni^{++}, Cu^{++}, Co^{++} and Fe^{++}—form a compound of the type $Me(HDm)_2$.

At first glance this conclusion may seem to contradict the observations of A. K. Babko et al. [7-9] on the influence of pH in the reaction of Cu^{++}, Fe^{++} and Co^{++} with H_2Dm. In our opinion, this discrepancy may be explained either by the fact that compounds of the type $Me(HDm)_2$ are the primary reaction products and undergo further change in solution, whereas in the conditions in the column the reaction stops at the stage of the formation of $Me(HDm)_2$, as a result of the adsorption of the latter by the carbon (similar phenomena have been observed in the chromatography of solutions by other investigators [24]) or by the fact that the carbon, by adsorbing predominantly the least polar complexes, causes a shift of the equilibrium in the direction of the formation of these compounds.

Our conclusion is confirmed by the fact that the compound of Co^{++} with H_2Dm formed in the column is decomposed by acid, whereas this does not take place in solution: the yellow coloration characteristic of the compound formed by Co^{++} and H_2Dm in solution undergoes no noticeable change on acidification [8] (see also [25]).

The factor determining the course of the process in the column is evidently the adsorption by the carbon of $Me(HDm)_2$ and not H_2Dm. Thus the compound of Co^{++} with H_2Dm, formed in a column consisting of a mixture of carbon and H_2Dm placed on a layer of pure carbon [12], is decomposed by acid in the same way as the compound formed by Co^{++} with the dimethylglyoxime adsorbed on the carbon. We confirmed indirectly the result obtained for Cu^{++}, by carrying out an experiment with a column consisting of a mixture of 3 g of carbon, treated with acid in the manner described above, with 0.3 g H_2Dm, on top of a layer of 3 g of the same carbon. In this case the ratio of the number of milliequivalents of acid liberated in the filtrate to the number of milliequivalents of Cu^{++} introduced into the column equalled 0.859, or 85.9%. When the reaction between Co^{++} and H_2Dm was carried out in similar conditions only approximately 1/5 of the cobalt introduced into the column went into the compound with H_2Dm. The much greater extent of the reaction of Co^{++} with H_2Dm adsorbed on the carbon may be explained both by the increase in the area of contact of the reagents and by the increased reactivity of the H_2Dm in the adsorbed condition.

SUMMARY

1. A method has been worked out for the study of complex formation between metal cations and organic reagents which are weak acids sparingly soluble in water. The method consists of the separation of the acid formed in the reaction from the complex compound, and is based on the different nature of adsorption on carbon of non-electrolytes and strong electrolytes and the dual character of the adsorption of strong mineral acids.

2. It has been established that when the reactions of Cu^{++}, Co^{++} and Fe^{++} with dimethylglyoxime are carried out in weakly acid medium in conditions where the complex compounds formed are adsorbed by carbon, the reaction products are compounds of the general formula $Me(HDm)_2$.

LITERATURE CITED

[1] A. K. Babko, J. Anal. Chem. 3, 284 (1948).

[2] L. A. Chugaev, Studies in the Field of Complex Compounds (Moscow, 1906).*

[3] L. A. Chugaev, J. Russ. Chem. Soc. 37, 610 (1905);Z. anorg. Chem. 46, 144 (1905).

[4] F. Feigl and H. Rubinstein, Ann. 433, 183 (1923).

[5] H. Diehl, The Applications of the Dioximes to Analytical Chemistry (1940).

[6] V. M. Peshkova, Sci.Repts.Moscow State University 78, 3 (1945).

[7] A. K. Babko and M. V. Korotun, J. Gen. Chem. 23, 1302 (1953) (T.p. 1367).**

[8] A. K. Babko and M. V. Korotun, J. Gen. Chem. 24, 597 (1954) (T.p. 609).**

[9] A. K. Babko and L. I. Dubovenko, J. Gen. Chem. 24, 751 (1954)(T.p. 759).**

[10] L. S. Nadezhina, Thesis (Rostov on Don 1953).

---

* In Russian.

** T.p. = C. B. Translation pagination

[11] V. A. Fialkov, Bull. Acad. Sci. USSR, Sect. Plat. 30, 5 (1955).

[12] A. M. Gurvich, T. B. Gapon and M. S. Rabinovich, Chem. Ind. 1956, No. 1, 31; T. B. Gapon, A. M. Gurvich, M. S. Rabinovich, V. V. Strukov and L. A. Usatova, Authors' Certificate No. 99924 (1954).

[13] F. Feigl, Chemistry of Specific, Selective and Sensitive Reactions (N.Y., 1949).

[14] J. Holluta, Monatsh. 40, 281 (1919); C. A. 14, 911 (1920).

[15] M. M. Dubinin, The Physicochemical Principles of Sorption Technique (1935); Miller, J. Phys. Chem. 36, 2967 (1932).*

[16] N. Schiloff, K. Tschmutoff, Z. Physik. Chem. A, 148, 233 (1930).

[17] Bruns and Frumkin, Z. Physik. Chem. A, 141, 141 (1929); A. Frumkin, Kolloid-Z 51, 123 (1930).

[18] N. Schiloff, G. Schatunowskaja, Tschmutoff, Z. Physik. Chem. 150, 31 (1930 L. K. Lepin); J. Phys. Chem. 5, 276 (1934).

[19] R. Burschtein, A. Frumkin and D. Lavrovskaja, Z. Physik. Chem. 150, 42 (1930) .

[20] N. A. Shiloy and L. K. Lepin, Reports of the Lomonosov Phys. Chem. Soc. 1, No. 1 (1919).

[21] M. M. Dubinin, Prog. Chem., 24, 513 (1955).

[22] L. M. Orlova, J. Anal. Chem. 5, 370 (1950); Yu. I. Usatenko and E. A. Klimkovich, Factory Lab. 19, 418 (1953).

[23] D. N. Strazhesko, Thesis, (Kiev, 1951).*

[24] E. N. Gapon and I. M. Belenkaya, Colloid J. 14, 323 (1952); (Tp. 353)**

[25] A. M. Gurvich, J. Anal. Chem. 11, 437 (1956) (T.p. 459)**

Received January 30, 1956

Academy of Sciences, Institute of Physical Chemistry, USSR

---

* In Russian.

** T.p. - C.B. Translation pagination

[15] A. [illegible]

[16] [illegible]

[17] F. Feigl, Chemistry [illegible]

[14] J. Hoffman, [illegible]

[15] M. M. Dubinin, [illegible]
Chem. [illegible] (1956).

[16] [illegible]

[17] [illegible]

[18] [illegible]

[19] [illegible]

[20] [illegible]

[21] [illegible]

[22] [illegible]

[23] [illegible]

[24] [illegible]

[25] A. M. [illegible]

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THE SYNTHESIS OF 1,1-DIPHENYL-4(OR 4,4)-ALKYL(OR ARYL)ALKANES VIA 3,3 DIPHENYLBUTYRONITRILE

A. D. Petrov and V. M. Vdovin

The synthesis of aliphatic-aromatic hydrocarbons of the above type has up till now been carried out by the reaction of phenyl Mg halide with esters of monobasic acids [1] or of adipic acid. However, whereas the first reaction led to the formation of alcohols in which only one of the radicals could be varied, the second gave a glycol with four identical radicals. In the present work a synthesis is suggested which enables compounds to be prepared with two different radicals out of four, which may lead to forms with lower freezing points.

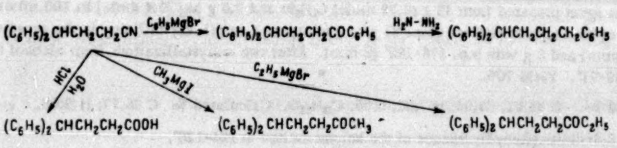
A. D. Grebenyuk and I. P. Tsukervanik [2] have recently carried out a Friedel-Crafts reaction with β-chloropropionitrile and chlorobenzene and also with benzene:

$$ClC_6H_5 + ClCH_2CH_2CN \xrightarrow{AlCl_3} ClC_6H_4CH_2CH_2CN.$$

We have succeeded in carrying out the condensation under similar conditions of β-trichloromethylpropionitrile with benzene, which takes place according to the equation:

$$Cl_3CCH_2CH_2CN + C_6H_6 \xrightarrow{AlCl_3} (C_6H_5)_2CHCH_2CH_2CN.$$

The 3,3-diphenylbutyronitrile obtained proved to be a convenient starting material for the synthesis both of the corresponding acid and of various ketones – intermediate products in the synthesis of the hydrocarbons. The reactions carried out in this investigation are represented by the following scheme:



3,3-Diphenylbutyric acid, which proves the structure of our nitrile, has been prepared earlier, but by a different method, from γ-phenylbutyrolactone and benzene using $AlCl_3$ [3]; 1,4,4-triphenylbutane has been synthesized for the first time; the ketones indicated in the scheme have also been obtained for the first time. 5,5-Diphenylpentanone-2 and 4,4-diphenylbutyrophenone formed derivatives with 2,4-dinitrophenylhydrazine immediately after addition of the reagent in the cold; 6,6-diphenylhexanone-3 gave a hydrazone with 2,4-dinitrophenylhydrazine after 24 hours.

In addition, attempts were made to carry out the reaction between $Cl_3CCH_2CH_2CN$ and different Grignard reagents (CH_3MgI, CH_3MgCl, C_6H_5MgBr), which were taken in different concentrations relative to the nitrile (from 1 to 7 moles for 1 mole of nitrile). In all cases the reaction took place in a undesirable direction, giving rise to condensation products insoluble in ether.

EXPERIMENTAL

Trichloromethylpropionitrile was prepared by the cyanoethylation of chloroform [4]. We prepared this product with m.p. 41° several times, in quantities of approximately 300 g in each experiment; it was established that the yield of 11% indicated by the authors may be raised to 18% (i.e. by approximately 60%, calculated from the chloroform reacting), if the ratio of acrylonitrile to chloroform taken is 1.5:1 and not 1:1. When moist or poorly ground alkali is used, or when the ratio is increased to 2:1, the yield is lowered.

3,3-Diphenylbutyronitrile. Molten $Cl_3CCH_2CH_2CN$ (200 g, 1.16 mole) was poured into 1060 g $AlCl_3$ (8.1 mole) and 1000 g C_6H_6 (13 mole); the mixture immediately became red in color and after 10-15 minutes vigorous evolution of HCl began and the reaction mixture became hot, so that it had to be cooled for the first 30 minutes. When the vigorous evolution of gas had ceased, the mixture was heated to the boiling point of the benzene and stirred for 18 hours*. The reaction mixture was then poured carefully onto ice. The aqueous layer was separated from the organic layer and extracted twice with 1000 ml benzene. The benzene extracts were combined, washed with a solution of sodium carbonate, then with water, and dried over Na_2SO_4. The benzene was distilled off and the thick black residue vacuum distilled. After a second distillation the fraction with b.p. 181° (3 mm) was collected and this crystallized after 24 hours. After three recrystallizations from ethyl alcohol the substance melted at 48.5-49°. Yield 78.5%.

Found %: C 86.27, 86.40; H 6.68, 6.91; N 6.11, 6.28 $C_{16}H_{15}N$. Calculated %: C 86.83; H 6.82; N 6.33.

5,5-Diphenylpentanone-2. 22 g (0.1 mole) 3,3-diphenylbutyronitrile in 100 ml ethyl ether was added with stirring over a period of 30 minutes to the Grignard reagent prepared from 42 g (0.3 mole) CH_3I and 7.2 g Mg (0.3 mole) in 100 ml absolute ethyl ether. The mixture was left overnight. The reaction mass was then poured into a two-liter flask containing a mixture of 400 g ice and 100 g concentrated HCl. The organic layer was separated,** and the aqueous layer extracted twice with 100 ml volumes of ether. The extracts were combined, washed, and dried with Na_2SO_4. The ether was distilled off and needle-like crystals were obtained by cooling the residue. Distillation under reduced pressure yielded 13 g oil with b.p. 180-183° at 6 mm, which crystallized in the receiver. After two recrystallizations from ethyl alcohol the substance melted at 86.5-87°. Yield 54.5%.

Found %: C 85.15, 85.25; H 7.65, 7.58. $C_{17}H_{18}O$. Calculated %: C 85.67; H 7.61.

The 2,4-dinitrophenylhydrazone of the ketone melted at 114-115°.

Found %: N 14.03, 13.80. $C_{23}H_{22}O_4N_4$. Calculated %: N 13.39.

6,6 Diphenylhexanone-3. 30 g (0.13 mole) of 3,3-diphenylbutyronitrile in 100 ml ether was poured into a Grignard reagent prepared from 43 g (0.39 mole) C_2H_5Br and 9.6 g Mg (0.4 mole) in 100 ml ether. Vacuum distillation of the reaction product gave: 21 g of a substance (an oil, crystallizing in the receiver) with b.p. 175-176° (2mm) and 3 g with b.p. 176-182° (2 mm). After two recrystallizations from alcohol the substance melted at 69-71°. Yield 70%.

Found %: C 86.01, 85.94; H 7.95, 8.09. $C_{18}H_{20}O$. Calculated %: C 85.77; H 7.98.

The 2,4-dinitrophenylhydrazone of the ketone melted at 124-125°.

Found %: N 13.26, 13.05. $C_{24}H_{24}O_4N_4$. Calculated %: N 12.95.

1,4,4-Triphenylbutanone-1 (4,4-diphenylbutyrophenone) was prepared similarly from 9.6 g (0.4 mole) Mg, 62 g (0.39 mole) C_6H_5Br and 30 g (0.13 mole) 3,3-diphenylbutyronitrile. The ether was distilled off and the product recrystallized three times from ether to give 15 g of substance with m.p. 91-92°. The mother liquor was vacuum distilled and 12 g of oil with b.p. 222° (2 mm), crystallizing in the receiver, was obtained.

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* When the tests were repeated it was found that heating for 12 hours was sufficient.

** In the synthesis of this ketone and the ketones described below, a greasy substance, insoluble in organic solvents, always separated on the walls of the separating funnel.

After one recrystallization from ether the substance melted at 91.5-92°. Yield 64.5%.

Found %: C 87.90, 88.05; H 6.78, 6.75. $C_{22}H_{20}O$. Calculated %: C 88.03; H 6.71.

The 2,4-dinitrophenylhydrazone of the ketone melted at 157-158°.

Found %: N 11.22, 11.25. $C_{28}H_{24}O_4N_4$. Calculated %: N 11.44.

3,3-Diphenylbutyric acid* was prepared by heating 22 g (0.1 mole) of 3,3-diphenylbutyronitrile under reflux with 100 ml concentrated hydrochloric acid. After 26 hours heating the hydrochloric acid was replaced 4 times with fresh material. The contents of the flask were then treated with 100 ml ether (two portions), the extracts combined and dried with Na_2SO_4. The ether was distilled off and the residue vacuum distilled; a fraction with b.p. 183-197° (1 mm) was obtained and later crystallized. After two recrystallizations from ethyl alcohol a product was obtained with m.p. 101-104.5°. Yield 24%.

Found %: C 79.90, 80.07; H 6.74, 6.77. $C_{16}H_{16}O_2$. Calculated %: C 79.98; H 6.73.

1,4,4-Triphenylbutane was prepared from 7.8 g 4,4-diphenylbutyrophenone (0.026 mole) and 3.5 g (0.073 mole) hydrazine hydrate, dissolved in 50 ml ethyl alcohol (catalyst Pd / $CaCO_3$). 4.7 g (63%) of a pale yellow viscous oil with b.p. 238-240° (16mm) was obtained, the main part of the substance distilled at 238° (16mm), n_D^{20} 1.5993, d_4^{20} 1.0317.

Found %: C 92.33, 92.20; H 7.67, 7.75. $C_{22}H_{22}$. Calculated %: C 92.25; H 7.74.

SUMMARY

1. 3,3-Diphenylbutyronitrile has been prepared for the first time, and from it various ketones have been synthesized (5,5-diphenylpentanone-2, 6, 6-diphenylhexanone-3, 4, 4-diphenylbutyrophenone).

2. A route to the synthesis of asymmetric aliphatic-aromatic hydrocarbons of the type 1,1-diphenyl-4 (or 4,4)-alkyl(or aryl) alkanes via 3,3-diphenylbutyronitrile has been suggested.

LITERATURE CITED

[1] K. Serijan and P. Wise, J. Am.Chem. Soc. 73, 5191 (1951).

[2] A. D. Grebenyuk and I. P. Tsukervanik, J. Gen. Chem., 25, 286 (1955) (T.p. 269)**

[3] G. Wittig, Ber. 64, 443 (1931).

[4] H. Bruson, W. Niederhauser, T. Riener and W. Hester, J. Am. Chem. Soc. 67, 601 (1945).

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Academy of Sciences, Institute of Organic Chemistry, USSR

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* Wittig, who synthesized this acid [3], isolated a substance with m.p. 105-106° in approximately 14% yield from the fraction 160-240° (12 mm).

** T.p. = C.B. Translation pagination

After recrystallization from [illegible]

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LITERATURE CITED

[1] M. [illegible] and [illegible], J. Am. Chem. Soc. [illegible]

[2] A. A. [illegible] and I. F. [illegible], J. Gen. Chem. [illegible]

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[4] [illegible]

Received January 7, 1958 [illegible]

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* Wittig, who synthesized this [illegible] from the fraction 150-160° (12 mm).

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THE REACTION OF CHLOROALKYLCHLOROSILANES WITH AROMATIC COMPOUNDS IN THE PRESENCE OF METALLIC ALUMINUM

E. A. Chernyshev and M. E. Dolgaya

In earlier communications [1,2] we have examined the question of silicoalkylation of aromatic compounds with different chloroalkylchlorosilanes in the presence of aluminum chloride. It has been shown that benzene, chlorobenzene and toluene may be silicoalkylated with chloromethyltrichlorosilane and also α- and β- chloroethylchlorosilanes in yields of up to 80%. It has also proved possible to use dichloromethyltrichlorosilane in this reaction. The most active compound of those studied was β-chloroethylethyldichlorosilane. The use of this last chloride opened up a new route to the synthesis of a series of organosilicon compounds with two hydrolyzable groups on the silicon.

One disadvantage of the reaction in the presence of $AlCl_3$ lies in the fact that in a number of cases a considerable amount of tar formation takes place, which makes the isolation of the reaction product difficult. Thus the products of the reaction of chloralkylchlorosilanes with diphenyl and with naphthalene could not be isolated because of tar formation. In addition, it is necessary to remove the $AlCl_3$ quantitatively in the form of its complex with $POCl_3$ before distillation to prevent tar formation in the distillation process.

Considerable interest has been attached to the search for a method of carrying out the reaction which would bring tar formation to a minimum. With this aim we also turned our attention to a study of the reaction of silicoalkylation in the presence of metallic aluminum. The use of metallic aluminum in the Friedel-Crafts reaction was first suggested by Radziewanowski [3] and afterwards used successfully by V. D. Azatyan [4], and also by N. G. Sidorova and by I. P. Tsukervanik et al. [5,6].

Metallic aluminum with alkyl halides first forms $RAlCl_2$, R_2AlCl or aluminum halides, which also are catalysts for the reaction. The compounds mentioned have evidently increased reactivity at the moment of formation, which enables the reaction to take place with the use of a very small quantity of aluminum.

The silicoalkylation of benzene with β-chloroethyltrichlorosilane in the presence of aluminum was successfully achieved and β-phenylethyltrichlorosilane was obtained in 72% yield. Practically no tar formed in the reaction mixture. It should be noted that although only 0.2 g of aluminum was introduced into the reaction mixture, a considerable part of it remained unused. The silicoalkyation of diphenyl and of naphthalene with β-chloroethyltrichlorosilane was also successfully carried out. In these cases tar formation took place, but not to such a great extent as when $AlCl_3$ is used.

β-(Phenoxyphenyl)-ethyltrichlorosilane was prepared from β-chloroethyltrichlorosilane and diphenyl oxide in 22.5% yield. For comparison purposes, the silicoalkylation of diphenyl oxide was carried out with β-chloroethyltrichlorosilane and β-chloroethylethyldichlorosilane in the presence of $AlCl_3$. It turned out that the yields of reaction product in these cases, as in the case of benzene, were approximately the same as when metallic aluminum was used. In all the reactions using aluminum the quantity of aluminum chloride formed was so small that its removal with $POCl_3$ was not necessary.

EXPERIMENTAL

1. The reaction of β-chloroethyltrichlorosilane with benzene in the presence of aluminum. 50 g of β-chloroethyltrichlorosilane, 78 g benzene and 0.2 g aluminum, in the form of fine turnings cut with a sharp knife from aluminum wire, were placed in a three-necked flask with mechanical stirrer, reflux condenser and thermometer. The reaction was started by heating the reaction mixture to 70°. The hydrogen chloride evolved was trapped in a Tishchenko flask with alkali solution. The course of the reaction was followed from the amount of hydrogen chloride absorbed. When 90-95% of the theoretical quantity of HCl had been absorbed the reaction was stopped. The precipitate which had formed and the unused aluminum were filtered off and the filtrate distilled. The distillation yielded 41.2 g β-phenylethyltrichlorosilane, yield 72.2%. When the same reaction was carried out with $AlCl_3$ the yield of β-phenylethyltrichlorosilane was 83%.

B.p. 82-83° (2.5 mm); 240-241° (760 mm), n_D^{20} 1.5170, d_4^{20} 1.2412, MR_D 58.30; calc. 58.04. [*]

2. The reaction of β-chloroethyltrichlorosilane with diphenyl in the presence of aluminum. The reaction was carried out in the apparatus used in Expt. 1. 50 g β-chloroethyltrichlorosilane, 54 g diphenyl and 0.1 g Al were taken for the reaction. The reaction was started by heating the mixture to 90° and then continued at a temperature of 50-60°. After two distillations, 26.1 g (33.8%) of β-(xenyl)-ethyltrichlorosilane was obtained.

B.p. 172-173° (3 mm), n_D^{20} 1.5830, d_4^{20} 1.2783, MR_D 82.45; calc. 82.25.

Found %: C 53.58, 53.69; H 4.22, 4.10; Si 8.35, 8.29; Cl 33.60, 33.28. $C_{14}H_{13}SiCl_3$. Calculated %: C 53.33; H 4.13; Si 8.87; Cl 33.67.

When the same reaction was carried out in the presence of $AlCl_3$ the product of silicoalkylation could not be isolated because of the formation of a very large quantity of tar.

3. The reaction of β-chloroethyltrichlorosilane with naphthalene in the presence of aluminum. The reaction was carried out in the apparatus used in Expt. 1. 50 g β-chloroethyltrichlorosilane, 52 g naphthalene and 0.27 g Al were taken for the reaction. The reaction was started by heating to 130-135°. Further reaction was continued at this temperature and stopped after 3-4 hours, during which a considerable amount of tar was formed. After two distillations 15.3 g (21.3%) of β-(naphthyl)-ethyltrichlorosilane was obtained.

B.p. 159-163° (3mm), n_D^{20} 1.5812, d_4^{20} 1.2977, MR_D 74.29; calc. 73.50.

Found %: Si 9.34, 9.26. $C_{12}H_{11}SiCl_3$. Calculated %: Si 9.67.

When the same reaction was carried out in the presence of $AlCl_3$ the silicoalkylation product could not be isolated because of tar formation.

4. The reaction of β-chloroethyltrichlorosilane with diphenyl oxide in the presence of aluminum. The reaction was carried out in the apparatus of Expt. 1. 1. 50 g β-chloroethyltrichlorosilane, 59.5 g diphenyl oxide and 0.2 g Al were taken for the reaction. The reaction was begun by heating the mixture to 130° and continued for a further 25 hours. 16.8 g (22.5%) of β-(phenoxyphenyl)-ethyltrichlorosilane was isolated by distillation.

B.p. 334-340°, n_D^{20} 1.5590, d_4^{20} 1.2668; MR_D 84.41; calc. 84.05.

Found %: C 50.44, 50.52; H 3.85, 3.89; Si 8.54, 8.36; Cl 31.80, 31.72 $C_{14}H_{13}OSiCl_3$. Calculated %: C 50.72; H 3.92; Si 8.45; Cl 32.07.

5. The reaction of β-chloroethyltrichlorosilane with diphenyl oxide in the presence of $AlCl_3$. The reaction was carried out in the apparatus of Expt. 1. 68 g β-chloroethyltrichlorosilane, 37 g diphenyl oxide and 1 g $AlCl_3$ were taken for the reaction. The reaction mixture was heated at 70-90° for 56 hours. 2 g $POCl_3$ and 30 ml isooctane were then added to the reaction flask and the mixture heated at 100° for 1 hour. The $POCl_3 \cdot AlCl_3$ complex which formed was filtered off and the filtrate distilled. The distillation yielded 23.7 g β-(phenoxyphenyl)-ethyltrichlorosilane, yield 30% (calculated from the diphenyl oxide).

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[*] Literature data [2]: b.p. 240.5° (739 mm), n_D^{20} 1.5188, d_4^{20} 1.2395.

B.p. 198-204° (13 mm), n^{20}_D 1.5590, d^{20}_4 1.2676, MR_D 84.36; calc. 84.05.

The product was methylated with CH_3MgBr. β-(Phenoxyphenyl)-ethyltrimethylsilane was obtained, yield 68%.

B.p. 310-314° (755 mm), n^{20}_D 1.5360; d^{20}_4 0.9840, MR_D 85.56; Calc. 85.16.

Found %: C 75.34, 75.44; H 8.52, 8.39; Si 10.00, 9.70 $C_{17}H_{22}OSi$. Calculated %: C 75.92; H 8.15; Si 10.30.

6. The reaction of β-chloroethylethyldichlorosilane with diphenyl oxide in the presence of $AlCl_3$. The reaction was carried out in the apparatus of Expt. 1. 35 g β-chloroethylethyldichlorosilane, 51 g diphenyl oxide and 1 g $AlCl_3$ were taken for the reaction. The diphenyl oxide, aluminum chloride and 5 g β-chloroethylethyldichloride were placed in the flask. The reaction began vigorously when the mixture was heated to 70-75°. When the reaction had started, the remaining 30 g of the chloride was added slowly (~1.5 hours) from a dropping funnel placed temporarily in the position of the thermometer. The reaction was stopped after 40 hours. 2 g $POCl_3$ and 30 ml isooctane were added. Heating was continued for 1 hour at 100° after which the $POCl_3 \cdot AlCl_3$ complex was filtered off and the filtrate distilled. 17.2 g (25.3%) of β-(phenoxyphenyl)-ethylethyldichlorosilane was obtained.

B.p. 231-232° (8 mm), n^{20}_D 1.5540, d^{20}_4 1.1644, MR_D 89.40; calc. 89.05.

Found %: C 59.30, 59.38; H 5.65, 5.64; Si 8.96, 8.74; Cl 21.46, 21.65. $C_{16}H_{18}OSiCl_2$. Calculated %: C 59.09; H 5.58; Si 8.63; Cl 21.80.

The substance was methylated using CH_3MgBr. β-(Phenoxyphenyl)-ethylethyldimethylsilane was obtained, yield 54%.

B.p. 214-215° (11 mm), n^{20}_D 1.5366, d^{20}_4 0.9831, MR_D 90.16; calc. 89.79.

Found %: C 75.92, 75.98; H 8.42, 8.40; Si 9.57, 9.72. $C_{18}H_{24}OSi$. Calculated %: C 76.05; H 8.45; Si 9.85.

7. The oxidation of β-(phenoxyphenyl)-ethyltrimethylsilane 6 g of β-(phenoxyphenyl)-ethyltrimethylsilane and 30 ml of nitric acid of specific gravity 1.110 were placed in a round-bottomed flask fitted with a reflux condenser. The mixture was boiled for 40 hours. A considerable quantity of crystals was formed. The organic layer and the crystals were separated; the aqueous layer was extracted with ether. The ether extracts were combined with the organic layer and the ether evaporated. The crystals were separated on a filter with a porous plate and the filtrate distilled. 1.8 g of the original substance was recovered. The crystals were recrystallized several times from a mixture of acetone and water. 2.3 g of crystals with m.p. 158° was obtained. According to the literature data [7], p-phenoxybenzoic acid melts at 159.5°. The greater part of the product of silicoalkylation of diphenyl oxide is thus the para-isomer.

SUMMARY

1. It has been shown possible to carry out the silicoalkylation of aromatic compounds with chloralkylchlorosilanes in the presence of metallic aluminum, and in this case the formation of tar takes place to a much lower extent than when $AlCl_3$ is used.

2. Naphthalene, diphenyl and diphenyl oxide have been silicoalkylated for the first time.

LITERATURE CITED

[1] A. D. Petrov, V. F. Mironov, V. A. Ponomarenko and E. A. Chernyshev, Proc. Acad. Sci. USSR 97, 687 (1954).

[2] A. D. Petrov, E. A. Chernyshev and M. E. Dolgaya, J. Gen. Chem. 25, 2469 (1955) (T.p. 2357)*

---

*T.p. = C.B. Translation pagination.

[3] C. Radziewanowski, Ber. 28, 1135 (1895).

[4] V. D. Azatyan, Proc. Acad. Sci. USSR 59, 901 (1948).

[5] N. G. Sidorova, I. P. Tsukervanik and Z. Abidova, Proc. Acad. Sci. Uzbekistan USSR 1953, No. 5,33.

[6] N. G. Sidorova, I.P. Tsukervanik and E, Pak, J. Gen. Chem. 24, 94 (1954) (T.p. 93)*

[7] Dictionary of Organic Compounds (1949), Vol. 3, 374.

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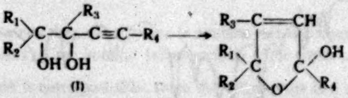
* T.p. = C.B. Translation pagination

A STUDY OF THE CHANGES UNDERGONE BY β-GLYCOLS OF THE ACETYLENE SERIES

I. THE SYNTHESIS AND CHANGES OF 2,4-DIMETHYL-6-PHENYLHEXYNE-5-DIOL-2,4

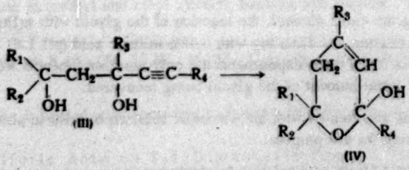
T. A. Favorskaya and L. A. Pavlova

It is known [1] that α-glycols of the acetylene series (I) are capable of reacting with sulfuric acid to form, together with other substances, compounds of the 2-hydroxyhydrofuran-2,5 series (II), exhibiting basic properties:



On the other hand it is known [2,3] that primary-tertiary and ditertiary γ-glycols react with sulfuric acid to give, as the first products of dehydration, β-ethylenic alcohols, which are easily isomerized to derivatives of tetrahydrofuran.

In connection with these data, interest was attached to the study of the changes undergone by β-glycols of the acetylene series (III) since the transformation of β-glycols to heterocyclic compounds would give substituted hydroxydihydropyrans (IV), which have been insufficiently studied up to the present:



It was also of interest to attempt to detect the first expected product of the reaction of the β-glycol (V) with sulfuric acid—the enyne alcohol (VI or VII)—and to show in this way that the first stage of this process takes place in the same way as the reaction of sulfuric acid with γ-glycols.

The study of the β-glycols of the acetylene series was begun with the most readily available 2,4-dimethyl-6-phenylhexyne-5-diol-2,4 (V). The glycol, synthesized according to the method of Iotsich from diacetone alcohol and phenylacetylene, was treated with sulfuric acid of the different concentrations 3, 6, 10, 20, 30% with heating to 70-100° for 1-2 hours. When the β-glycol was treated with dilute sulfuric acid (3 and 6%), the greater part of the glycol was recovered unchanged. Small amounts of acetone and isopropenylphenylacetylene (VIII) were isolated from the reaction products.

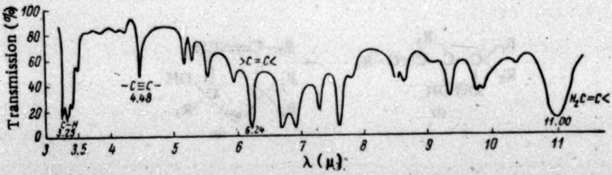
The acetone was determined as the 2,4-dinitrophenylhydrazone. Isopropenylphenylacetylene was first obtained by Skosarevsky by the dehydration of dimethylphenylacetylenylcarbinol [4]. The formation of the same compound during the preparation of the chlorohydrin of dimethylphenylacetylenylcarbinol was observed by A. I. Zakharova and Z. I. Sergeeva [5]. The authors of these works did not give a proof of the structure of the hydrocarbon, considering that in their experiments no other compound could be formed. The hydrocarbon isolated by us has constants agreeing satisfactorily with those given in the literature. For a confirmation of its structure the substance was oxidized and the infrared absorption spectrum examined.*

The spectrum was taken on a IKS-2 instrument, while the layer thickness was 0.1 mm. The spectrum up to 5.5 μ was taken with a LiF prism and beyond that with one of NaCl.

The curve shows the clearly defined maxima of intensity of absorption characteristic of the acetylene link (4.48μ) and of the isopropenyl group (valency frequency 3.25 μ, deformation frequency 11 μ).

The curve obtained is on the whole similar to the infrared absorption curve for phenylacetylene and vinylacetylene.

The absorption curve thus confirms the structure of the substance as isopropenylphenylacetylene.



When the acid concentration, temperature and length of heating are increased, the quantity of acetone and isopropenylphenylacetylene in the reaction products is increased. Thus, for example, when the glycol is treated with 3% sulfuric acid for 50 minutes at 70-80°, approximately 20% acetone and enyne hydrocarbon are formed; when the glycol is treated with 10% sulfuric acid on the boiling water bath the yield of acetone and enyne hydrocarbon reaches 90%. In the tests with 20 and 30% sulfuric acid the reaction is accompanied by considerable tar formation, which is evidently the result of condensation of the isopropenylphenylacetylene [4].

With the aim of obtaining the enine alcohol, the reaction of the glycol with sulfuric acid was carried out in very mild conditions, by heating and distilling with 0.12% sulfuric acid (pH 1.6) and by shaking with 40% sulfuric acid in the cold, but in all these experiments the only reaction products were acetone and the enyne hydrocarbon, a greater or lesser amount of the glycol being recovered.

The β-glycol obtained was also treated with an alcoholic solution of sulfuric acid. 4 and 17% sulfuric acid in 96% ethyl alcohol was used for this purpose.

In the experiments with 4% sulfuric acid solution in alcohol we managed to isolate, in addition to acetone and isopropenylphenylacetylene, a highboiling fraction which boiled over a wide range, gave a qualitative reaction for hydroxyl and ethoxy groups and for the double bond, gave no sign of the presence of a carbonyl group, and had a composition and molecular weight close to those of the glycol. This fraction is evidently a mixture of the original glycol with the products of etherification (most probably the partial ether) and dehydration. The mixture obtained was treated with 6% aqueous sulfuric acid to hydrolyze the ethers formed. The product obtained from this experiment had b.p. 139-142° (2 mm) and had similar properties to the product with b.p. 135-138° (1 mm), formed by the action of a 17% sulfuric acid solution in alcohol on the glycol. According to the analysis data this fraction approaches closest of all to the product of dehydration of the glycol—the enyne alcohol (VI or VII). A slight trace of the ethoxy-containing compound was also detected, which may also explain the somewhat low analysis results. When this fraction was oxidized, α-hydroxyisobutyric, benzoic and benzoylformic acids and acetone were obtained.

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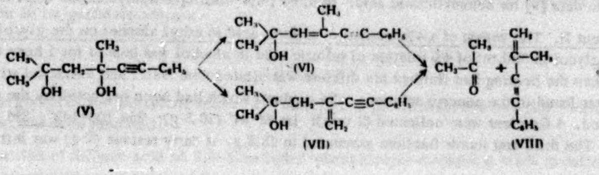
* The spectrum was investigated by Prof. A. A. Petrov, for which we wish to express to him our deep appreciation.

The results obtained enable us to put forward the following scheme for the changes undergone by 2,4-dimethyl-6-phenylhexyne-5-diol-2,4 (V). When the glycol is treated with sulfuric acid, dehydration takes place first of all. A very great number of experiments have shown that in the glycols of the acetylene series the greatest mobility is shown by the hydroxyl situated in the α-position relative to the triple bond [1,6,7]; two dehydration products (VI and VII) are therefore possible. The oxidation data show that the main product of the dehydration is the enyne alcohol—2,4-dimethyl-6-phenylhexene-3-enyne-5-ol-2 (VI).



The enyne alcohol obtained then decomposes to acetone and isopropenylphenylacetylene (VIII). The same products may be obtained by the ketonic decomposition of the enyne alcohol (VII).

This conversion scheme is quite probable, since the dehydration of β-glycols when heated with acids is well known, while the ketonic decomposition of the unsaturated alcohol also has analogs in the literature [8].

The formation of a mixture of enyne alcohols when 2,4-dimethyloctene-7-yne-5-diol-2,4—a β-glycol with the vinylacetylene radical—is distilled over potassium bisulfate was observed by I. N. Nazarov and I. V. Torgov [7]. They also observed the formation in this experiment of a mixture of unsaturated hydrocarbons.

EXPERIMENTAL

2,4-Dimethyl-6-phenylhexyne-5-diol-2,4 was synthesized by the method of Iotsich from diacetone alcohol and phenylacetylene and obtained in the form of needle-like crystals with m.p. 63-64° in 70-88% yield. The substance was soluble in methyl and ethyl alcohol, benzene and acetone. It may be recrystallized from ligroin and petroleum ether.

Found %: C 77.20; H 8.40; OH 15.82. M 215. $C_{14}H_{18}O_2$. Calculated %: C 77.03; H 8.31; OH 15.60. M 218.3.

When the substance is heated with potassium carbonate, phenylacetylene is formed.

The Action of Sulfuric Acid on 2,4-Dimethyl-6-Phenyl-Hexyne-5-Diol-2,4

Experiment I. 6 g of the glycol was heated on a boiling water bath with stirring with 60 ml 10% sulfuric acid for 2 hours. The reaction mixture was extracted with ether, the ether extract washed with sodium carbonate, and with water and dried with sodium sulfate. Acetone was detected (1.5 g) in the aqueous solution and the wash water by the formation of the 2,4-dinitrophenylhydrazone. The residue remaining after the distillation of the ether was vacuum distilled. 3.5 g (90%) of a colorless mobile liquid, which proved to be the enyne hydrocarbon—isopropenylphenylacetylene—was collected at 81-82° (1 mm).

B.p. 81-82° (1 mm) n_D^{20} 1.5835, d_4^{20} 0.9247, MR_D 51.36. $C_{11}H_{10}F_4\equiv$. Calc. 46.93.

Found %: C 92.63, H 7.35. $C_{11}H_{10}$. Calculated %: C 92.93; H 7.04.

The oxidation of isopropenylphenylacetylene. 47 g potassium permanganate was used for the oxidation of 7 g of the hydrocarbon. The oxidation was carried out to begin with using 1% $KMnO_4$ solution (200 ml) and afterwards the salt was added in the form of a finely ground powder. No neutral oxidation products were obtained. The solution of salts obtained was evaporated on a water bath and acidified with sulfuric acid to liberate CO_2 and benzoic acid, which gave no freezing point depression with a known sample of benzoic acid. The volatile acids were steam distilled. The solution, with odor of acetic acid, was heated with silver carbonate and the salt obtained was found to contain 64.01% of silver (calculated for CH_3COOAg – 64.67% Ag). The solution of the non-volatile acids was extracted with ether; after drying and removal of the solvent a thick dark acid remained which gradually crystallized and was pressed out on a porous plate. M.P. 63-64°.

Equiv. neutr. 166; calculated for benzoylformic acid 150.

The 2,4-dinitrophenylhydrazone of the acid melted at 197°.

Literature data [9] for benzoylformic acid: m.p. 66°; 2,4-dinitrophenylhydrazone m.p. 196-197°.

Experiment II. The action of a 4% solution of sulfuric acid in ethyl alcohol on the glycol. A solution of 35 g of the glycol in 350 ml of 4% solution of sulfuric acid in alcohol was heated for 1 hour with stirring at 70-80°. When the heating had finished the mixture was diluted with water and extracted with ether. 4.5 g of acetone was found in the aqueous solution. The products which had been extracted by the ether were vacuum distilled. 4 fractions were collected (2 mm): 1st 82-84° (10.5 g); 2nd 100-142°; 3rd 142-150°; 4th 150-152°. The third and fourth fractions amounted to 15.2 g. A tarry residue (2 g) was left in the distillation flask.

Analysis of the fraction with b.p. 150-152° (2 mm) : n_D^{20} 1.5355, d_4^{20} 0.9768.

Found %: C 78.54; H 9.06; OH 8.77; OC_2H_5 10.86. M 224. $C_{14}H_{18}O_2$ (V). Calculated %: C 77.03; H 8.31; OH 15.60. M 218.3. $C_{16}H_{22}O_2$ (partial ether of the glycol). Calculated %: C 78.09; H 8.99; OH 6.90. OC_2H_5 18.30. M 246.3. $C_{14}H_{16}O$ (VI). Calculated %: C 83.94; H 8.05; OH 8.49. M 200.3.

Experiment III. The action of aqueous sulfuric acid on the fraction 142-152° (2 mm). 9 g of the high-boiling fraction obtained in the previous experiment was heated with 6% sulfuric acid for one and a half hours at 80-90°. 0.5 g of acetone was found in the aqueous solution. The high-boiling products were vacuum distilled. This yielded 1 g of the enyne hydrocarbon (VIII) with b.p. 78-80° (2 mm) and 6 g of a product with b.p. 139-142° (2 mm).

Analysis of the fraction 139-142° (2 mm): n_D^{20} 1.5532, d_4^{20} 0.9780, MR_D 65.45. $C_{14}H_{16}OF_4\vDash$. Calc. 62,31. $C_{16}H_{22}O_2F_3\vDash$. Calc. 73.66.

Found %: C 83.18; H 8.60; OH 8.02; OC_2H_5 3.30. M 199. $C_{14}H_{16}O$ (VI). Calculated %: C 83.94; H 8.05; OH 8.49; M 200.3. $C_{16}H_{22}O_2$. Calculated %: C 78.09; H 8.99; OH 6.90; OC_2H_5 18.30. M 246.3.

The oxidation of the fraction 139-142° (2 mm). 2 g of the product was added to a solution of 3.7 g potassium permanganate in 200 ml water. The oxidation was carried out with shaking at room temperature. When the reaction mixture had gone colorless after 2 hours a further 0.3 g of oxidant was added. The precipitate of manganese dioxide was filtered off and washed with hot water and ether. The neutral products were steam distilled from the filtrate and wash waters. The acetone was determined. The solution of salt was evaporated to dryness and the residue broken up with sulfuric acid. This precipitated benzoic acid which was identified by a mixed melting point test with a known sample of benzoic acid. A small quantity of the filtrate from the separation of the benzoic acid was added to solutions of 2,4-dinitrophenylhydrazine sulfate and phenylhydrazine hydrochloride. The 2,4-dinitrophenylhydrazone precipitated gave no melting point depression when mixed with the known 2,4-dinitrophenylhydrazone of benzoylformic acid [9]. The yellow phenylhydrazone obtained melted at 153°, which agrees with the literature data for benzoylformic acid [10].

The solution of acids was extracted with ether. The ether-soluble acids partly crystallized. Part of the crystals was separated and washed with benzene on a porous plate. The needle-shaped crystals obtained gave no melting point depression with a known sample of α-hydroxyisobutyric acid [11]. The remaining ether-soluble acids were converted to the silver salts.

Found %: Ag 1st fraction 46.91; 2nd fraction 47.24; 3rd fraction 49.09; 4th fraction 50.86, 50.83 C_6H_5COOAg. Calculated %: Ag 47.15; $(CH_3)_2COHCOOAg$ %: Ag 51.19; CH_3COOAg%: Ag 64.67.

The acids which did not dissolve in the ether were steam distilled. Formic acid was detected in the distillate by the formation of a precipitate with mercuric chloride solution and by the darkening of ammoniacal silver oxide solution.

The formation of α-hydroxyisobutyric and benzoylformic acids on oxidation shows that the main constituent of the part of the product with b.p. 139-142° (2 mm) is the enine alcohol–2,4-dimethyl-6-phenylhexene-3-yne-5-ol-2 (VI).

The oxidation of the other possible dehydration product– 2-methyl-4-methylene-6-phenylhexyne-5-ol-2 (VII)– would have led to the formation of β-hydroxyisovaleric acid. This acid was not detected by us, which indicates that the enyne alcohol (VII) is either absent from the products of the reaction of the glycol or else is present in insignificant amount.

SUMMARY

1. The β-glycol of the acetylene series–2,4-dimethyl-6-phenylhexyne-5-diol-2,4– which is not described in the literature, has been prepared.

2. The action of sulfuric acid on 2,4-dimethyl-6-phenylhexyne-5-diol-2,4 leads to dehydration of the glycol with subsequent decomposition of the enyne alcohol to give acetone and isopropenylphenylacetylene.

LITERATURE CITED

[1] E. D. Venus-Danilova, L. A. Pavlova, V. I. Serkova and E. P. Brichko, Trans Leningrad Lensoviet. Tech. Inst. 1954, No. 30, 38.

[2] T. A. Favorskaya and O. V. Sergievskaya, J. Gen. Chem. 25, 1509 (1955) (T.p. 1459).*

[3] T. A. Favorskaya and N. P. Ryzhova, J. Gen. Chem. 26, 423 (1956) (T.p. 447).*

[4] M. P. Skosarevsky, J. Russ. Chem. Soc. 37, 645 (1905).

[5] A. I. Zakharova and Z. I. Sergeeva, J. Gen. Chem. 18, 1324 (1948).

[6] T. A. Favorskaya and A. N. Shirshova, J. Gen. Chem. 19, 177 (1949) (T.p. 159).*

[7] I. N. Nazarov and I. V. Torgov, J. Gen. Chem. 18, 1480 (1948).

[8] Grignard and Chambret, Compt. rend. 182, 299 (1926); T. A. Favorskaya and Sh. A. Friedman, J. Gen. Chem. 18, 2080 (1948); E. D. Venus-Danilova and V. I. Serkova, J. Gen. Chem. 24, 994 (1954) (T.p. 993).*

[9] Dictionary of Organic Compounds, Vol. 1, 231.

[10] Elbers, Ann. 227, 341 (1885).

[11] Beilst. 4th ed. Vol. III. p. 313.

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The Lensoviet Institute of Technology, Leningrad,
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* T.p. = C.B. Translation pagination.

[illegible] Fig. 18 [illegible]

CH₃COOMg [illegible]

The [illegible] [illegible] distribution, the formation [illegible] [illegible] ester [illegible].

The [illegible] [illegible] hexane-1-yne [illegible] (V).

The oxidation of the [illegible] [illegible] (VII) [illegible] which [illegible] or else is present in insignificant amounts.

SUMMARY

1. The [illegible] in the literature, has been prepared.

2. The action of [illegible] with subsequent [illegible].

LITERATURE CITED

[1] [illegible] Tech. Inst. 1954, No. 22, 88.

[2] [illegible]

[3] I. A. [illegible] Chem. [illegible]

[4] M. F. Shostakovskii, [illegible]

[5] [illegible]

[6] I. A. [illegible] and [illegible] J. Gen. Chem. 16, [illegible]

[7] [illegible]

[8] Coquet and [illegible] Chem. [illegible]

[9] Dictionary of Organic Compounds, Vol. [illegible]

[10] Beilst. Supp. [illegible]

[11] [illegible]

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1,1,3,3-TETRAALKOXYPROPANES

T. V. Protopopova and A. P. Skoldinov

The importance in synthesis of malondialdehyde as the first and simplest representative of the series of β-dicarbonyl compounds is obvious. At the present time β-ethoxyacroleindiethylacetal is used as the starting material for the preparation of malondialdehyde [1]. Notices have recently appeared in the patent literature on the preparation of 1,1,3,3-tetraalkoxypropanes [2-5], which are the full acetals of malondialdehyde and in advertisement announcements on their use [6].

In a systematic study of the reactions of unsaturated compounds leading to formation of β-dicarbonyl compounds or of their functional derivatives [7], we have undertaken the synthesis of the full acetals of malondialdehyde and the study of their chemical behavior. In the present work we describe the properties of a series of 1,1,3,3-tetraalkoxypropanes (I), where R = CH_3, C_2H_5, iso-C_3H_7, n-C_4H_9, prepared by the reaction of vinyl ethers with the esters of orthoformic acid in the presence of catalysts of the Friedel-Crafts type. This reaction is similar to the well-studied reaction of vinyl ethers with acetals which leads to the formation of alkoxyacetals or of the products of the further addition to them of one or several molecules of the vinyl ether [8]; in this reaction a considerable excess of acetal relative to the vinyl ether (molar ratio not less than 3:1) is required to obtain a high yield of the "monomeric" alkoxyacetal.

The addition of an orthoformate likewise does not stop at the formation of the 1,1,3,3-tetraalkoxypropane (I); the latter in turn may add on across the double bond, forming the 1,1,3,5,5,-pentaalkoxypentane (II) and the products of the further reaction of the latter with the vinyl ether:

$$HC(OR)_3 + CH_2{=}CHOR \xrightarrow{(C_2H_5)_2O\cdot BF_3} \underset{(I)}{(RO)_2CHCH_2CH(OR)_2}$$

$$(I) + CH_2{=}CHOR \xrightarrow{(C_2H_5)_2O\cdot BF_3} \underset{(II)}{(RO)_2CHCH_2CH(OR)CH_2CH(OR)_2}$$

The reaction was carried out by us with different molar ratios of orthoformate and vinyl ether; in this case the yield of the "mono-adduct" is not so dependent on the use of an excess of the orthoformate as it is in the case of the addition of the acetals. This may be explained by the fact that the orthoester function may be considerably more easily ionized by the action of the boron trifluoride than the acetal function. The relatively greater reactivity of the orthoester function has also been confirmed by the results of a competitive reaction of equimolecular amounts of ethyl orthoformate, 1,1,3,3-tetraethoxypropane and vinyl ethyl ether, in which the main reaction product was the "mono-adduct"(I).

The reaction of methyl orthoformate with vinyl ethyl ether (in the molar ratio 1:1) gave, in addition to the expected 1,1,3-trimethoxy-3-ethoxypropane (yield 47%), 1,1,3,3-tetramethoxypropane (yield 10%), whose formation may be explained by the exchange of alkoxy groups between the tetraalkoxypropane formed and the still unreacted orthoester in the presence of the boron trifluoride. Evidence for this suggestion is provided by the fact that with a molar ratio of the components of 4:1, only 1,1,3,3-tetramethoxypropane was isolated from the reaction mixture (yield 55%).

In the majority of the reactions carried out the ether complex of boron trifluoride was used as catalyst, but in the case of the preparation of 1,1,3,3-tetraethoxypropane, completely satisfactory results were obtained using stannic chloride, ferric chloride or the ether complex of aluminum chloride.

The standard conditions for the synthesis of the 1,1,3,3-tetraalkoxypropanes are given in the experimental part under the preparation of 1,1,3,3-tetraethoxypropane. The yields, physical properties and analysis results for the compounds obtained are given in Table 1.

By the further reaction of 1,1,3,3-tetraalkoxypropanes with the vinyl ethers in the presence of the ether complex of boron trifluoride, we have prepared a series of 1,1,3,5,5-pentaalkoxypentanes (II) (R = CH_3, C_2H_5, iso-C_3H_7, n-C_4H_9), which are also of interest as synthetic intermediates. In this case a considerable excess of the tetraalkoxypropane is necessary; but even when these conditions are observed the yields remain low and a considerable amount of products with higher molecular weight is formed, and these have not as yet been further studied. The physical properties and analysis results for the 1,1,3,5,5-pentaalkoxypentanes obtained are given in Table 2.

EXPERIMENTAL

Starting products. The orthoformates were prepared in the usual way [9]; the vinyl ethers were prepared by the superalkylation of vinyl butyl ether in the presence of mercury acetate [10].

1,1,3,3-Tetraethoxypropane. 18 g (0.25 mole) of vinyl ethyl ether was added dropwise to a mixture of 74 g (0.5 mole) of ethyl orthoformate and 0.35 ml of the ether-boron trifluoride complex, heated to 33°, the temperature during the addition being kept below 45°. When all the vinyl ether had been added (which required 15 minutes), the mixture was stirred for 1 hour, 2.5 g of anhydrous sodium carbonate was added and mixing continued for a further 3 hours at room temperature. The precipitate was filtered off and the filtrate fractionated in vacuo in the presence of a small quantity of sodium carbonate. 31.3 g of unchanged ethyl orthoformate and 43.9 g (80 %, calculated on the vinyl ether) of 1,1,3,3-tetraethoxypropane, b. p. 87-88°(6 mm) were obtained.

When the experiment was carried out in similar conditions, but using as catalyst a solution of 0.5 g anhydrous aluminum chloride in 12 ml ether, 0.5 g of stannic chloride or 0.25 g of freshly distilled ferric chloride, the yields obtained were 70, 80 and 72%, respectively.

When the experiment described above was carried out with molar ratios of orthoester to vinyl ether of 4:1, 3:1, 2:1 and 1:1, the yields were 81, 79, 80 and 75 % respectively.

1,1,3-Trimethoxy-3-ethoxypropane. 21.6 g of vinyl ethyl ether was added rapidly (over a period of 8 minutes) to a mixture of 31.8 g methyl orthoformate and 0.15 ml of the ether-BF_3 complex, heated to 30°; the temperature was maintained at 35-38° by external cooling. Immediately after the addition of all the vinyl ethyl ether, 2 g of anhydrous sodium carbonate was added and the mixture stirred for 3 hours at room temperature. The salts were filtered off and the filtrate fractionated on a 45 cm column packed with glass rings. The following fractions were collected at 12 mm: 1st 66-67° – 4.9 g, slightly impure 1,1,3,3,-tetramethoxypropane; 2nd 69-74° – 2.0 g; 3rd 74.5-75° – 25.0 g (47%) 1,1,3-trimethoxy-3-ethoxypropane. •

A considerable amount of higher-boiling products was obtained, but these were not further studied.

When the experiment was carried out with a molar ratio of methyl orthoformate to vinyl ethyl ether equal to 4:1, the only product obtained on fractionation of the reaction mass was 1,1,3,3-tetramethoxypropane (55 %).

B. p. 69-70° (13 mm), n_D^{20} 1.4070, d_4^{20} 0.9895.

Found %: C 51.45; H 9.82. $C_7H_{16}O_4$. Calculated %: C 51.19; H 9.81.

The competitive reaction of the vinyl ether with a mixture of ethyl orthoformate and 1,1,3,3-tetraethoxypropane. 10.8 g of vinyl ethyl ether was added gradually to a mixture of 22.2 g ethyl orthoformate, 33 g tetraethoxypropane and 0.25 ml of the ether-boron trifluoride complex, heated to 30°; the temperature of the reaction mass was kept at 45-50° by external cooling. The solution obtained was given the usual treatment (see above); the following fractions

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• For constants see Table 1.

TABLE 1

1,1,3,3-Tetraalkoxypropanes $(R'O)_2CHCH_2CH(OR)(OR')$

R	R'	Substance obtained	Formula	Yield (%, calculated on the vinyl ether)	Boiling point*	d_4^{20}	n_D^{20}	MR_D		Analysis (%)				Remarks
								Found	Calculated	Found**		Calculated		
										C	H	C	H	
CH_3	CH_3	1,1,3,3-Tetramethoxypropane	$C_7H_{16}O_4$	60	66° (12mm)	0.9920	1.4067	40.79	41.09	50.93	9.65	51.19	9.81	Literature data [4]: b.p. 70-75° (15 mm)
C_2H_5	CH_3	1,1,3-Trimethoxy-3-ethoxypropane	$C_8H_{18}O_4$	47	74.5—75 (12mm)	0.9675	1.4077	45.40	45.71	53.86	10.01	53.91	10.17	At the same time, a 10% yield, calculated on the vinyl ether, was obtained of somewhat impure 1,1,3,3-tetramethoxypropane: b.p. 66-67° (12 mm), d_4^{20} 0.9840, n_D^{20} 1.4073
C_2H_5	C_2H_5	1,1,3,3-Tetraethoxypropane	$C_{11}H_{24}O_4$	80	87—88 (6mm)	0.9190	1.4105	59.38	59.57	60.30	10.92	60.00	10.67	Literature data [11]: b.p. 77-78° (3 mm), d_4^{25} 0.916, n_D^{25} 1.4101
iso-C_3H_7	iso-C_3H_7	1,1,3,3-Tetraisopropoxypropane	$C_{15}H_{32}O_4$	53	107.5 (5mm)	0.8851	1.4140	77.95	78.04	65.06	11.66	65.18	11.67	The substance was unstable and decomposed rapidly on storage
iso-C_4H_9	n-C_4H_9	1,1,3,3-Tetra-n-butoxypropane	$C_{19}H_{40}O_4$	80	138—139 (2mm)	0.8860	1.4290	96.43	96.51	68.77	12.23	68.62	12.12	Literature data [3]: b.p. 128° (0.5 mm), $d_{15.6}^{20}$ 0.883, n_D^{20} 1.4266

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* Uncorrected boiling points are given throughout.

** The mean values from two determinations are given.

TABLE 2

1,1,3,5,5-Pentaalkoxypentanes $(RO)_2CHCH_2CH(OR)CH_2CH(OR)_2$

R	Formula	Yield (%, calculated on the vinyl ether)	Boiling point	d_4^{20}	n_D^{20}	MR_D		Analysis (%)			
						Found	Calculated	Found***		Calculated	
								C	H	C	H
CH_3	$C_{10}H_{22}O_5$	24.0	79—80° (3mm)	1.0080	1.4238	56.22	56.59	54.18	9.94	54.03	9.97
C_2H_5	$C_{15}H_{32}O_5$*	34.0	111—112 (2mm)	0.9316	1.4212	79.61	79.68	61.68	11.07	61.61	11.07
iso-C_3H_7	$C_{20}H_{42}O_5$**	24.0	118—120 (2 mm)	0.9030	1.4238	102.30	102.77	65.78	11.43	66.28	11.67
n-C_4H_9	$C_{25}H_{52}O_5$	23.0	189—190 (3mm)	0.9020	1.4386	126.08	125.87	69.19	11.76	69.38	12.11

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* Literature data [3]: b.p. 90° (1 mm), d_{20}^{28} 0.9233, n_D^{30} 1.4180.

** The substance is unstable, decomposing rapidly on storage.

*** The mean values of two determinations are given.

were obtained during the fractionation: 1st up to 85° (6 mm) – 5.3g; 2nd 86-88° (6 mm) – 51.1 g, n^{20}_{D} 1.4098, d^{20}_{4} 0.9200; 3rd 113-114° (2 mm) – 2.8 g, n^{20}_{D} 1.4210, d^{20}_{4} 0.9362.

The second fraction proved to be pure 1,1,3,3-tetraethoxypropane (the orthoester used amounted to 56% of the theoretical). The 3rd fraction was 1,1,3,5,5-pentaethoxypentane (the 1,1,3,3-tetraethoxypropane used amounted to 6.4% of the theoretical).

1,1,3,5,5-Pentaethoxypentane. 3.6 g (0.05 mole) of vinyl ethyl ether was added gradually to a mixture of 55 g (0.25 mole) of 1,1,3,3-tetraethoxypropane and 0.3 ml of the ether boron trifluoride complex, heated to 30°, during which addition the temperature rose to 45°; when the vinyl ether had been added, the mixture was stirred at room temperature for 1 hour, 2 g of anhydrous sodium carbonate added and the mixture stirred for a further 2.5 hours. The salts were removed and the filtrate fractionated in vacuo on a 50 cm fractionating column fitted with a complete condensation head. This yielded 16.8 g of the original 1,1,3,3-tetraethoxypropane (b. p. 87-89° at 6 mm) and 5 g (34%) of 1,1,3,5,5-pentaethoxypentane, which after a second distillation boiled at 111-112° (2 mm) (see Table 2).

SUMMARY

1. A description has been given of the properties of a series of 1,1,3,3-tetraalkoxypropanes $(RO)_2CHCH_2CH(OR)_2$ (where: R = CH_3, C_2H_5, iso-C_3H_7 and n-C_4H_9), prepared by the reaction of esters of orthoformic acid with vinyl ethers in the presence of catalysts of the Friedel-Crafts type.

2. It has been shown that the orthoesters add on to the double bond more readily than do the acetals.

3. A description has been given of the properties of a series of 1,1,3,5,5-pentaalkoxypentanes $(RO)_2CHCH_2CH(OR)CH_2CH(OR)_2$ (where: R = CH_3, C_2H_5, iso-C_3H_7 and n-C_4H_9).

LITERATURE CITED

[1] R Huttel, Ber. 74, 1825 (1941).

[2] U. S. Patent 2,500,486; C. A. 1950, 5379; U. S. Patent 2,502,433; C. A. 1950, 6430; U. S. patent 2,517,543; C. A. 1951, 1166; U. S. patent 2,527,533; C. A. 1951, 1622.

[3] U. S. patent 2,556,312; C. A. 1952, 1031;

[4] U. S. patent 2,549,076; C. A. 1949, 4291 .

[5] Japanese patent 4321 ('52); C. A. 1954, 5211.

[6] Chem. Eng. News 33 (29) 3028 (1955).

[7] T. V. Protopopova and A P. Skoldinov, J. Gen. Chem. 26, 3355 (1956).*

[8] R. I. Hoagein and D. H. Hirsh, J. Am. Chem. Soc. 71, 3468 (1949); R. Paul and S. Tchelitcheff, Bull., Soc. Chim. 1950, 1155; M. F. Shostakovsky, V. A. Gladyshevskaya, Bull. Acad. Sci. USSR, Div. Chem. Sci. 140, 344 (1955).*

[9] P. P. T. Sah and T. S. Ma, J. Am. Chem. Soc. 54, 2964 (1932) .

[10] British Patent 709,106; C. A. 1955, 10,360.

[11] S. M. McElwain and R. L. Clarke, J. Am. Chem. Soc. 69, 2657 (1947).

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Institute of Pharmacology and Chemotherapy,
Academy of Medical Sciences, USSR

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β- AMINOVINYL KETONES

VII. THE REACTION OF β-CHLOROVINYL KETONES WITH TERTIARY AMINES

V. T. Klimko, A. Ya. Khorlin, V. A. Mikhalev, A. P. Skoldinov and N. K. Kochetkov

β - Chlorovinyl ketones are capable of undergoing many reactions with the replacement of their highly mobile chlorine atom by other groups and the formation thereby of β-substituted alkylvinyl ketones [1]. This reaction, which we have called ketovinylation, proceeds particularly smoothly with ammonia [2] and with secondary amines [3], leading to the formation of β-amino-and β-dialkylaminovinyl ketones. The quaternary ammonium salts corresponding to these compounds have, however, remained unknown. In this connection it must be borne in mind that quaternary ammonium salts containing a ketonvinyl radical cannot be prepared by the reaction of alkyl halides with β-dialkylaminovinyl ketones, since alkylation of the latter takes place with transfer of the reactive center to the α-carbon atom [4, 5]. At the same time, quaternary ammonium salts of the type $(RCOCH{=}CHNCHN^{+}R_3)X^{-}$

are of fundamental interest in connection with the question of the interaction between the carbonyl group and the nitrogen atom in the system O=C– C=C– N [4], while they may also be used as convenient starting materials for a number of syntheses.

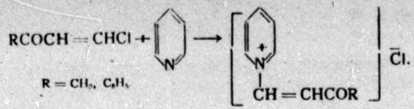
We have made a study of the reaction of β-chlorovinyl ketones with tertiary amines with the aim of obtaining quaternary ammonium salts containing the ketovinyl radical. A. Ya. Yakubovich and E. N. Merkulova [6] obtained a crystalline substance by the reaction of methyl β-chlorovinyl ketone with pyridine; they did not, however, make any definite suggestions as to its structure. As was later shown in a work from our laboratory [7], this compound was undoubtedly a quaternary pyridinium salt.

The reaction of β-chlorovinyl ketones with tertiary amines proved to be of a fairly general character. Both reagents react spontaneously in a medium of inert organic solvents (absolute alcohol, benzene, chloroform). The reaction takes place so vigorously that to obtain the required results it must be carried out in dilute solutions or with efficient cooling. The quaternary salt is precipitated from the reaction mixture in the crystalline condition and is separated in good yield (70-90 %) by the general methods;

$$RCOCH{=}CHCl + NR'_3 \rightarrow [RCOCH{=}CHN^{+}R'_3]\ Cl^{-},$$

where: $R{=}CH_3,\ C_3H_7,\ C_6H_5,\ o\text{-}BrC_6H_4,\quad p\text{-}O_2NC_6H_4;\ R'{=}CH_3,\ C_2H_5$

The reaction takes place equally well with alkyl β-chlorovinyl ketones (methyl and propyl β-chlorovinyl ketones) and with their aromatic analogs (phenyl, o-bromophenyl and p-nitrophenyl β-chlorovinyl ketones). We used trimethylamine and triethylamine as the tertiary amines. It was found by us that the reaction proceeds so smoothly that it can be used for the isolation of β-chlorovinyl ketones without preliminary purification of the latter from the reaction mixture in which they are prepared [8]. The reaction takes place just as smoothly with pyridine; the corresponding N-(β-ketoalkenyl)-pyridinium chlorides are obtained in the same conditions in yields of 90-95 %;



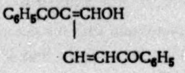
The trialkyl-(β-ketoalkenyl)-ammonium and N-(β-ketoalkenyl)-pyridinium salts are crystalline hygroscopic substances, readily soluble in water and insoluble in the majority of non-polar solvents; certain of them are soluble in chloroform. When well purified, they may be stored for fairly long periods, although the pyridinium salts darken with time; The β-ketoalkenylammonium salts readily exchange their ionic chlorine atom for other anions. This reaction is carried out in the usual way, i.e., by the reaction of the chloride with the salt of the appropriate acid in alcohol, and was carried out by us for the preparation of triethyl-(3-ketobutenyl)-ammonium iodide from the corresponding chloride:

$$CH_3COCH{=}CH\overset{+}{N}(C_2H_5)_3\ Cl^- + KI \rightarrow [CH_3COCH{=}CH\overset{+}{N}(C_2H_5)_3]\ I^- + KCl.$$

Interesting results were obtained on the hydrolysis of one of the salts obtained – triethyl-(β-benzoylvinyl)-ammonium chloride — by heating with aqueous bicarbonate solution. Instead of the expected 1,3,5-triacylbenzene which is usually formed in the hydrolysis of β-chlorovinyl ketones and their derivatives [1], we obtained in this case a crystalline substance with m. p. 152-153°, as a result of the condensation of the hydroxymethylene ketone formed as an intermediate product. This substance gave a coloration with ferric chloride and decolorized potassium permanganate instantly. The analysis and molecular weight determination indicated the composition $C_{18}H_{14}O_3$. We did not undertake a special study of the structure of this substance, but its properties and molecular formula lead to one of two suggested structures (I or II):

$C_6H_5COCH{=}CHOCH{=}CHCOC_6H_5$

(I)



$$\begin{array}{l}C_6H_5CO\underset{|}{C}{=}CHOH\\ \quad CH{=}CHCOC_6H_5\end{array}$$

(II)

EXPERIMENTAL

Triethyl-(β-acetylvinyl)-ammonium chloride. A solution of 10.1 g triethylamine in 50 ml absolute ether was added to a solution of 10.45 g methyl β-chlorovinyl ketone in 50 ml absolute ether, the mixture left for 3 hours, the precipitated crystals filtered off and dried in vacuo. Yield 18.5 g (90%); colorless crystals, m. p. 160° very readily soluble in water, insoluble in ether and benzene.

Found %: Cl 17.32, 17.52. $C_{10}H_{20}ONCl$. Calculated %: Cl 17.23.

Triethyl-(β-butyrylvinyl)-ammonium chloride. Prepared similarly from 12.0 g propyl β-chlorovinyl ketone and 9.3 g triethylamine in 30 ml ether. Yield 19.1 g (89.7 %); very hygroscopic colorless crystals, m. p. 96-98° (in sealed capillary).

Found %: Cl 15.90. $C_{12}H_{24}ONCl$. Calculated %: Cl 15.17.

Triethyl-(β-benzoylvinyl)-ammonium chloride was prepared similarly from 20.0 g phenyl β-chlorovinyl ketone and 14.65 g triethylamine in 50 ml ether. Yield 27 g (84 %); colorless crystals with m. p. 135-135.5° (with decomp. in sealed capillary).

Found %: Cl 13.38; 13.43. $C_{15}H_{22}ONCl$. Calculated %: Cl 13.24.

Triethyl-[β-(o-bromobenzoyl)-vinyl]-ammonium chloride was prepared similarly from 0.5 g o-bromophenyl β-chlorovinyl ketone and 0.25 g triethylamine in 10 ml ether. Yield 0.5 g (71%); yellowish crystals, m. p. 180° (with decomp).

Found %: Cl 10.47, 10.46. $C_{15}H_{21}ONClBr$. Calculated %: Cl 10.23.

Triethyl-[β-(p-nitrobenzoyl)-vinyl]-ammonium chloride was prepared similarly from 0.3 g p-nitrophenyl β-chlorovinyl ketone and 0.14 g triethylamine in 10 ml ether Yield 0.31 g (70.0 %). Orange leaflets with m. p. 132° (with decomp.) after recrystallization from 50% alcohol, sparingly soluble in water, readily soluble in alcohol.

Found %: N 8.47, 8.45; Cl 11.47, 11.47. $C_{15}H_{21}O_9N_2Cl$. Calculated %: N 8.25; Cl 11.34.

Trimethyl-(β-acetylvinyl) -ammonium chloride. Solutions of 4 g methyl β-chlorovinyl ketone in 10 ml benzene and 25 ml trimethylamine in 20 ml benzene were cooled to 0° and mixed, after which the mixture was left to stand for 5 hours at room temperature. The precipitate was filtered off and dried over paraffin. Yield 5.3 g (87 %); colorless hygroscopic crystals with m. p. 150° (with decomp.).

Found %: Cl 21.38; 21.06. $C_7H_{14}ONCl$. Calculated %: Cl 21.67.

N-(β-acetylvinyl)-pyridinium chloride. 4.05 g pyridine was added with cooling and stirring to a solution of 5 g methyl β-chlorovinyl ketone in 30 ml absolute ether, the mixture left for several hours at room temperature, the precipitated salt filtered off and dried in vacuo. Yield 8.3 g (92%); colorless crystals, decomposition temperature 163-165° (rapid heating in a sealed capillary).

Found %: Cl 19.46; 19.03. $C_9H_{10}ONCl$. Calculated %: Cl 19.31 .

N-(β-benzoylvinyl)-pyridinium chloride was prepared similarly from 9.0 g phenyl β-chlorovinyl ketone and 4.3 g pyridine in 30 ml ether. Yield 12.5 g (94 %); colorless hygroscopic crystals, decomposition temperature 171-172° (rapid heating in a sealed capillary).

Found %: Cl 14.42; 14.53. $C_{14}H_{12}ONCl$. Calculated %: Cl 14.43.

Triethyl -(β-acetylvinyl)-ammonium iodide. A solution of 0.9 g sodium iodide in 5 ml methanol was added to a solution of 1.0 g triethyl-(β-acetylvinyl)-ammonium chloride in 5 ml methanol. The mixture was left for 2 hours at room temperature, the precipitate of sodium chloride filtered off, the methanol removed from the filtrate in vacuo over sulfuric acid and the crystalline residue recrystallized from anhydrous alcohol. Yield 1.0 g (69.2 %); colorless prisms with m. p. 138-140° (with decomp.), readily soluble in water, crystallizes from alcohol.

Found %: I) (Fajan's method) 42.98, 43.10. $C_{10}H_{20}ONI$. Calculated %: I 42.71.

The hydrolysis of triethyl-(β-benzoylvinyl)-ammonium chloride. A solution of 5.5 g triethyl-(β-benzoylvinyl)-ammonium chloride and 3.4 g sodium bicarbonate in 40 ml water was heated for 24 hours at 50°. The yellowish crystalline precipitate obtained was cooled, filtered off and recrystallized from 80 ml methanol. This yielded 2.6 g of colorless needle-like crystals with m. p. 152-153° .

Found %: C 77.56, 77.66; H 5.12. 5.12. M 293 (determined cryoscopically in benzene).
$C_{18}H_{14}O_3$. Calculated %: C 77.68; H 5.07. M 278.3.

The substance rapidly decolorized a solution of potassium permanganate in acetone and gave an intense cherry-red coloration with a solution of ferric chloride in methanol.

SUMMARY

1. Trialkyl-(β-ketoalkenyl)-ammonium chlorides and β-ketoalkenylpyridinium chlorides have been prepared in good yields by the reaction of β-chlorovinyl ketones with tertiary aliphatic amines and pyridine respectively, in a medium of inert solvents.

2. The ionic halogen in the substances obtained is easily exchanged for another anion on treatment with a salt of the appropriate acid.

LITERATURE CITED

[1] N. K. Kochetkov, Prog. Chem. 24, 32 (1955).

[2] A. N. Nesmeyanov, N. K. Kochetkov and Ya. V. Dombrowsky, Bull. Acad. Sci. USSR, Div. Acad. Sci. 1955, 179 (T. p. 157). *

[3] N. K. Kochetkov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1953, 991 (T. p. 883)* .

[4] N. K. Kochetkov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1954, 47 (T. p. 37).*

[5] N. K. Kochetkov, M. G. Ivanova and A. N. Nesmeyanov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1956, 676 (T. p.687)*.

[6] A. Ya. Yakubovich and E. N. Merkulova, J. Gen. Chem. 16, 55 (1946).

[7] A. N. Nesmeyanov, N. K. Kochetkov and M. I. Rybinskaya, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1950, 350.

[8] V. T. Klimko, N. K. Kochetkov, V. A. Mikhalev, A. P. Skoldinov and A. Ya. Khorlin, Authors' Certificate No. 103767 of Nov. 12, 1955.

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Institute of Pharmacology and Chemotherapy,
Academy of Medical Sciences, USSR

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* T. p. = C. B. Translation pagination.

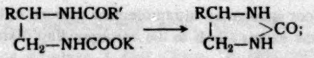
THE MECHANISM OF THE HOFMANN REACTION

S. I. Kanevskaya* and D. S. Yaskina

The mechanism of the Hofmann reaction has up to the present time been the subject of a great deal of research and discussion. In particular, there are several opinions on the question of the closing of the glyoxalidone ring which is formed when the Hofmann reaction is carried out with amides of acylated β-aminoacids.

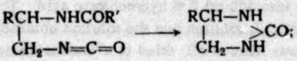
Different authors consider that the closure of this ring takes place:

1) by the formation of a carbamic acid and the simultaneous removal of the acyl group as the salt of the carboxylic acid [1]:



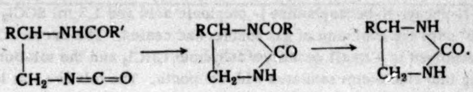
$$\begin{array}{l}\mathrm{RCH{-}NHCOR'}\\ |\\ \mathrm{CH_2{-}NHCOOK}\end{array} \longrightarrow \left.\begin{array}{l}\mathrm{RCH{-}NH}\\ |\\ \mathrm{CH_2{-}NH}\end{array}\right\rangle \mathrm{CO};$$

2) by the formation of the isocyanate with the simultaneous removal of the acyl group [2]



$$\begin{array}{l}\mathrm{RCH{-}NHCOR'}\\ |\\ \mathrm{CH_2{-}N{=}C{=}O}\end{array} \longrightarrow \left.\begin{array}{l}\mathrm{RCH{-}NH}\\ |\\ \mathrm{CH_2{-}NH}\end{array}\right\rangle \mathrm{CO};$$

3) by the formation of the isocyanate as a result of its intramolecular isomerization, while the removal of the acyl group is a secondary process [3-6]:



$$\begin{array}{l}\mathrm{RCH{-}NHCOR'}\\ |\\ \mathrm{CH_2{-}N{=}C{=}O}\end{array} \longrightarrow \left.\begin{array}{l}\mathrm{RCH{-}NCOR}\\ |\\ \mathrm{CH_2{-}NH}\end{array}\right\rangle \mathrm{CO} \longrightarrow \left.\begin{array}{l}\mathrm{RCH{-}NH}\\ |\\ \mathrm{CH_2{-}NH}\end{array}\right\rangle \mathrm{CO}.$$

In order to examine further the mechanism of the Hofmann reaction we carried out the reaction with β-phenyl-β-(N-phenyl-N-benzoylamino)-propionamide (I), since the absence of a hydrogen atom on the nitrogen of the amino group of this amide means that the formation of the corresponding glyoxalidone is possible only by the first of the schemes described above. In fact compound (I) can be converted into the glyoxalidone only if the latter is formed via the potassium salt of the carbamic acid according to the following scheme:

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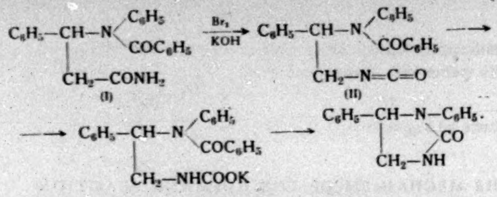

The original β-phenyl-β-(N-phenylamino)-propionic acid was prepared by us from its lactam, which was prepared in turn from benzalaniline and bromoacetic ester by the Reformatsky reaction [7].

We had to work out special conditions for the benzoylation of β-phenyl-β-(N-phenylamino)-propionic acid, since the action of benzoyl chloride in pyridine [8-10] gave negative results both in the cold and with heating. The benzoylation could only be achieved by the action of benzoyl chloride in a medium of quinoline bases. In this way we obtained β-phenyl-β-(N-phenyl-N-benzoylamino)-propionic acid, which was converted to the amide (I) via the hydrochloride.

In the study of the reaction between β-phenyl-β-(N-phenyl-N-benzoylamino)-proprionamide (I) and potassium hypobromite, we did not once detect the formation of the corresponding glyoxalidone. After a careful examination of the reaction products the only substance to be isolated was a material whose properties and analysis data corresponded to β-phenyl-β-(N-phenyl-N-benzoyl)-ethylenediamine.

Consequently, the intermediate isocyanate (II), as a result of the absence of a hydrogen atom on the nitrogen of the amino group, does not undergo an intramolecular closure to form the glyoxalidone, but is hydrolyzed under the influence of the excess alkali to the corresponding diamine.

EXPERIMENTAL

The preparation of β-phenyl-β-(N-phenyl-N-benzoylamino)-propionic acid. 6 g β-phenyl-β-(N-phenylamino) propionic acid was dissolved in 9 ml of quinoline bases (b. p. 187-189°) and 6 ml of benzoyl chloride added to the solution, during which the mixture evolved heat. After 26 hours the mixture was poured dropwise into 100 ml 2 % hydrochloric acid. The pale grey precipitate obtained was decanted, dissolved in 7% $NaHCO_3$ solution and the solution obtained acidified with 20% hydrochloric acid. The precipitate obtained was filtered off, dried in a vacuum desiccator treated with benzene and recrystallized twice from dilute alcohol (1:2). The substance melted at 163-164°. Yield 6.02 g (70%).

Found equiv 346. $C_{22}H_{19}O_3N$. Calculated equiv 345.4.

The preparation of β-phenyl-β-(N-phenyl-N-benzoylamino)-propionamide. 2.4 g β-phenyl-β-(N-phenyl-N-benzoylamino)- propionic acid and 1.5 ml $SOCl_2$ were heated for 2 hours 15 minutes at 38-40° until the evolution of gas bubbles had ceased. The excess $SOCl_2$ was distilled off in vacuo, the residue dissolved in a small quantity of anhydrous $CHCl_3$ and the solution obtained poured with uninterrupted stirring into chloroform saturated with ammonia. The mixture was left for 12 hours, the precipitate of NH_4Cl obtained filtered off and the filtrate evaporated. The thick yellow oil obtained crystallized when treated with ether. The residue was filtered off and recrystallized twice from dilute alcohol (1:2); m. p. of the amide 155-156°.

Found %: C 76.71; H 5.91; N 7.80. $C_{22}H_{20}O_2N_2$. Calculated %: C 76.72; H 5.86; N 8.13.

The action of potassium hypobromite on β-phenyl-β-(N-phenyl-N-benzoylamino)-propionamide. 0.3 g β-phenyl-β-(N-phenyl-N-benzoylamino)-propionamide was added to a freshly prepared solution of potassium hypobromite (0.606 g KOH, 2.91 ml water and 0.093 ml Br_2).

40 minutes after the reaction had begun the amide had been converted into an oily yellow colored substance, which after 1-1.5 hours began to solidify and acquired an orange color. On further shaking no change was observed. The reaction lasted 2 hours. The mixture was then heated on the water bath at a temperature of 80° for 6 minutes. The mixture was cooled, the dark yellow precipitate filtered off, treated several times with toluene, the slight undissolved residue again filtered off and the filtrate evaporated. This yielded 0.16 g of pale yellow material, which after recrystallization from dilute alcohol (1:1) melted at 168.5-169.5° corresponding to β-phenyl-β-(N-phenyl-N-benzoyl)-ethylenediamine.

Found %: C 79.81; C 79.81; H 6.39; N 8.82. $C_{21}H_{20}ON_2$. Calculated %: C 79.71; H 6.38; N 8.85.

SUMMARY

The reaction of β-phenyl-β-(N-phenyl-N-benzoylamino)-propionamide with potassium hypobromite has been studied and it has been established that this reaction leads not to the corresponding glyoxalidone but to β-phenyl-β-(N-phenyl-N-benzoyl)-ethylenediamine. From this it follows that the glyoxalidones are formed not as a result of intramolecular cyclization of intermediate carbamic acid salts but as a result of intramolecular isomerization of intermediate isocyanates.

LITERATURE CITED

[1] S. Kanewskaja, J. Progr. Chem. 132, 335 (1932).

[2] P. Karrer and A. Schlosser, Helv. Chim Acta, 6, 411 (1923).

[3] V. M. Rodionov and V. K. Zvorykina, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1943, 216.

[4] V. M. Rodionov and V. K. Zvorykina, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1950, 608.

[5] V. M Rodionov and V. V. Kiseleva, J. Gen. Chem. 18, 1905 (1948).

[6] V. M. Rodionov and V. V. Kiseleva, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1951, 57.

[7] H. Gilman and M. Specter, J. Am. Chem. Soc. 65, 2255 (1943).

[8] G. Heller, Ber. 37, 3115 (1904).

[9] G. Heller, Ber. 40, 117 (1907).

[10] P. Freundler, Chem. Zentr. 1904, II. 97.

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40 minutes after the reaction had begun the [illegible] had been converted into an oily yellow-colored substance, which after 1-1½ hours began to [illegible]. On further [illegible] no change was observed. The reaction [illegible]. The mixture was [illegible] at a temperature of 80° for 4 minutes. The mixture was cooled, the dark yellow [illegible] filtered off, treated several times with benzene, the [illegible] and the filtrate evaporated. The yield 0.10 g of pale yellow [illegible], which after recrystallization from [illegible] melted at 108.5-109.5°, corresponding to 4-phenyl-6-[illegible].

Found %: C 76.81; C 76.82; H 6.29; [illegible]. Calculated %: [illegible] N 5.88

SUMMARY

The reaction of 4-phenyl-6-[illegible] has been studied and it has been [illegible] to 4-phenyl-6-[illegible]. [illegible] are formed [illegible] of intramolecular [illegible].

LITERATURE CITED

[1] [illegible]

[2] [illegible]

[3] V. M. Rodionov and [illegible]

[4] V. M. Rodionov and V. [illegible]

[5] V. M. Rodionov and [illegible]

[6] V. M. Rodionov and V. V. [illegible]

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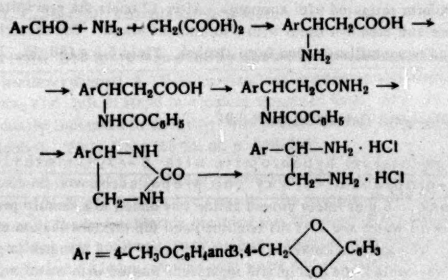
THE SYNTHESIS OF SUBSTITUTED ETHYLENEDIAMINES BY THE HOFMANN REACTION

S. I. Kanevskaya* and D. S. Yaskina

Substituted ethylenediamines have in recent times attracted increased attention from chemists and pharmacologists as substances with extremely valuable biological properties. Many ethylenediamine derivatives exhibit, as is well known, an antihistamine and also a depressant action. The salts of ethylenediamine are widely used as diuretic agents. When the methods of synthesizing substituted ethylenediamines are considered, it is seen from the literature data [1, 2] that in the majority of cases the synthesis of these compounds is fairly complicated as a result of the many stages involved and partly also because of the difficulty of obtaining the starting materials.

In 1932 S. I. Kanevskaya [3] suggested a method, which was extremely convenient from the preparative point of view, for the preparation of arylethylenediamines, based on the decomposition of the corresponding glyoxalidones with hydrochloric acid. The latter are also easily formed from the amides of N-acylated β-aminoacids by the Hofmann reaction, as was established by S. I. Kanevskaya and V. M. Rodionov. This therefore seemed to us to be an appropriate route for the synthesis of phenylethylenediamine derivatives [4] containing methoxy and methylenedioxy groups in the phenyl radical. The synthesis of 4-methoxy- and 3,4-methylenedioxyphenylethylenediamine was achieved according to the following scheme:


ArCHO + NH₃ + CH₂(COOH)₂ → ArCHCH₂COOH →
NH₂
→ ArCHCH₂COOH → ArCHCH₂CONH₂ →
NHCOC₆H₅
NHCOC₆H₅
→ ArCH—NH
CO →
CH₂—NH
Ar—CH—NH₂ · HCl
CH₂—NH₂ · HCl
Ar = 4-CH₃OC₆H₄ and 3,4-CH₂
O
O
C₆H₃

The original β-(3,4-methylenedioxyphenyl)- and β-(4-methoxyphenyl)-β-aminopropionic acids were prepared by us according to the widely known method of V. M. Rodionov [5-13] and afterwards benzoylated with benzoyl chloride in alkaline medium [14] and converted (via the ester or the hydrochloride) to the corresponding amides. When the Hofmann reaction was carried out with the amides of β-(3,4-methylenedioxyphenyl)-β-(N-benzoylamino)-propionic and β-(4-methoxyphenyl)-β-(N-benzoylamino)-propionic acids, we isolated respectively 5-(3,4-methylenedioxyphenyl)-glyoxalidone together with 5-(3,4-methylenedioxyphenyl)-1,3,4-oxadiazolone-(2)** and 5-(4-methoxyphenyl)-glyoxalidone together with 5-(4-methoxyphenyl)-1,3,4-oxadiazolone-(2). When 5-(3,4-methylenedioxyphenyl)-glyoxalidone was heated with concentrated hydrochloric acid in the conditions described earlier by S. I. Kanevskaya [3], charring took place.

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** It should be noted that these compounds, which were already prepared by us in the first half of 1951, were described by V. M. Rodionov and V. V. Kiseleva [15] in the middle of 1953. The methods of separation worked out by us, however, differ from those described by V. M. Rodionov and V. V. Kiseleva.

Only after milder hydrolysis conditions had been found (dilute HCl) for the hydrolysis of this glyoxalidone and also for 5-(4-methoxyphenyl-glyoxalidone, did it prove possible to obtain the dihydrochlorides of 3,4-methylenedioxyphenylethylenediamine and 4-methoxyphenylethylenediamine.

Pharmacological tests, carried out in the School of Pharmacology of the Moscow Pharmaceutical Institute by M. M. Nikolaeva and P. M. Subbotin, showed that 3,4-methylenedioxyphenylethylenediamine dihydrochloride, taken internally, brought about an increase in the blood pressure of cats and rabbits, its action, however, being approximately 500 times weaker than that of adrenalin. At the same time 4-methoxyphenylethylenediamine dihydrochloride, in the same doses, proved to be incapable of altering the blood pressure.

EXPERIMENTAL

I. β-(3,4-Methylenedioxyphenyl)-β-(N-benzoylamino)-propionic acid. 6.0 g β-(3,4-methylenedioxyphenyl)-β-aminopropionic acid was dissolved in 10% KOH solution and 12.6 g benzoyl chloride added in small portions from a separating funnel, with constant shaking and cooling, to the solution obtained. 10% KOH solution was also added in small portions from another separating funnel (100 ml in all) so that the mixture had always a faintly alkaline reaction. When the benzoylation was complete, 200 ml ether was added and the aqueous solution acidified with HCl (1:1) with constant shaking until acid to congo red. The benzoyl derivative collected at the boundary between the aqueous and ether layers as a white powder. After 12 hours the precipitate was separated and washed with ether. Yield 6.3 g (70%). The substance obtained was twice recrystallized from dilute alcohol (1:1); m. p. 196-197°.

Found %: N 4.40 Equiv 312.3. $C_{17}H_{15}O_5N$. Calculated %: N 4.47. Equiv 313.3.

β-(3,4-methylenedioxyphenyl)-β-(N-benzoylamino)-proprionamide. 6.0 g β-(3,4-methylenedioxyphenyl)-β-(N-benzoylamino)-propionic acid and 4.2 ml $SOCl_2$ were heated at 40° until the evolution of bubbles of gas had ceased. The excess $SOCl_2$ was distilled off in vacuo, the hydrochloride obtained dissolved in a small quantity of anhydrous chloroform, and this solution added with constant shaking and cooling to chloroform saturated with ammonia. After 12 hours the precipitate obtained was filtered off, washed with ether and then 3-4 times with a solution of alkali. The material obtained was ground up with water, filtered off and recrystallized twice from alcohol. Yield 5.3 g (88 %). The amide obtained melted at 266-267°.

Found %: N 8.78. $C_{17}H_{16}O_4N_2$. Calculated %: N 8.97.

The reaction of potassium hypobromite with β-(3,4-methylenedioxyphenyl)-β-(N-benzoylamino)-propionamide. a) The preparation of 5-(3,4-methylenedioxyphenyl) -glyoxalidone. 5 g of finely ground amide was added to a freshly prepared solution of hypobromite (11.2 g KOH, 54 ml water and 1.71 ml bromine) and the mixture shaken until fully dissolved. The reaction lasted 5 hours. The solution obtained was heated at 80° for 6 minutes (a precipitate came down at 75°). The mixture was cooled, the precipitate separated, washed with water and treated several times with alcohol. Part of the substance, insoluble in alcohol (0.4 g) proved to be the original amide. Removal of the solvent from the alcoholic filtrate yielded 5-(3,4-methylenedioxyphenyl)-glyoxalidone. After two recrystallizations from water it melted at 212-213°; yield 1.72 g (56%).

Found %: C 58.54; H 4.87; N 13.91. $C_{10}H_{10}O_3N_2$. Calculated %: C 58.24; H 4.89; N 13.58.

b) The preparation of 5-(3,4-methylenedioxyphenyl)-1,3,4-oxadiazolone-(2). The alkaline filtrate obtained after the separation of the glyoxalidone (see above) was treated with HCl (1:1) until acid to congo red. The material which precipitated was treated with steam and the residue

(0.5 g) recrystallized from dilute alcohol (1:2), m. p. 242-243° (1.4 g benzoic acid was isolated from the aqueous distillate).

Found %: C 52.71; H 2.99; N 13.52. $C_9H_6O_4N_2$. Calculated %: C 52.44; H 2.93; N 13.59.

3,4-Methylenedioxyphenylethylenediamine dihydrochloride. 0.5 g 5-(3,4-Methylenedioxyphenyl)-glyoxalidone and 25 ml HCl (1:2) were heated on a boiling water bath for 1 hour, 45 minutes. The solution was then evaporated, the dry residue dissolved in water, the slight residue (unreacted glyoxalidone) filtered off and the filtrate again evaporated to dryness. The 3,4-methylenedioxyphenylethylenediamine dihydrochloride obtained (0.5 g, 81%) was purified by precipitation from anhydrous alcohol with absolute ether.

Found %: C 42.53; H 5.53; N 10.85. $C_9H_{12}O_2N_2 \cdot 2HCl$. Calculated %: C 42.71; H 5.57; N 11.07.

II. **β-(4-Methoxyphenyl)-β-(N-benzoylamino)-propionic acid.** 7.5 g β-(4-methoxyphenyl)-β-aminopropionic acid was added to a small quantity of 10% KOH solution, and benzoyl chloride (16.13 g) was added dropwise from a separating funnel with constant shaking and cooling at the same time KOH solution (10.32 g in 100 ml water) was added in small portions from another separating funnel. When 300 ml ether and hydrochloric acid (to an acid reaction to congo red) had been added, a white substance was precipitated at the boundary between the aqueous and the ether layers. After 5 hours this substance was filtered off and washed with ether. Weight 10.8 g (94%), m. p. 200-201°.

Found %: N 4.46. $C_{17}H_{17}O_4N$. Calculated %: N 4.68.

Ethyl β-(4-methoxyphenyl)-β-(N-benzoylamino)-propionate. 5.0 g conc. H_2SO_4 was added to a solution of 5.0 g β-(4-methoxyphenyl)-β-(N-benzoylamino)-propionic acid in 100 ml anhydrous alcohol and the mixture heated on the water bath for 3 hours. 60 ml of alcohol were then distilled off (in vacuo) and the residue poured into 50 ml cold water, and a white precipitate was obtained. 7% $NaHCO_3$ solution was then added until faintly alkaline and the precipitate filtered off after 2 hours. Yield 4.9 g (90%). After two recrystallizations from alcohol the substance melted at 120.5-121.5°.

Found %: N 4.03. $C_{19}H_{21}O_4N$. Calculated %: N 4.28.

The preparation of β-(4-methoxyphenyl)-β-(N-benzoylamino)-propionamide. a) 3 g of ethyl β-(4-methoxyphenyl)-β-(N-benzoylamino)-propionate was dissolved in absolute alcohol saturated with ammonia, and left to stand in a tightly stoppered flask. After 14 days a white precipitate appeared and this gradually increased in quantity. The precipitate was filtered off after a further 5 days and recrystallized from alcohol. Yield 1.5 g (55%); m. p. 258-259°.

b) 4 g β-(4-methoxyphenyl)-β-(N-benzoylamino)-propionic acid and 2.8 ml $SOCl_2$ were heated at 38-40° until the evolution of gas bubbles had ceased. The reaction lasted for 4 hours. The excess $SOCl_2$ was distilled off in vacuo. The hydrochloride obtained was dissolved in dry chloroform and the solution poured with constant shaking and cooling into chloroform saturated with ammonia. A white precipitate was obtained, filtered off after 12 hours, washed with water and recrystallized twice from alcohol. M. p. 258-259°; yield 3.9 g (97.8%).

Found %: N 9.63. $C_{17}H_{18}O_3N_2$. Calculated %: N 9.39.

The reaction of potassium hypobromite with β-(4-methoxyphenyl)-β-(N-benzoylamino)-propionamide. a) **The preparation of 5-(4-methoxyphenyl)-glyoxalidone.** 2.5 g of finely ground amide was added to a freshy prepared hypobromite solution (5.83 g KOH, 28 ml water and 0.9 ml bromine) and the mixture shaken until completely dissolved. The reaction lasted for 3 hours. The solution obtained was heated at 80° for 6 minutes (a precipitate began to form at 45° and increased markedly at 75°). The mixture was cooled, the precipitate filtered off and washed with water. The substance obtained was treated several times with alcohol. The part which did not dissolve

(0.1 g) proved to be the original amide. Removal of the solvent from the alcoholic filtrates yielded 0.75 g of the glyoxalidone, which after two recrystallizations from water melted at 149-150°.

Found %: N 14.54. $C_{10}H_{12}O_2N_2$. Calculated %: N 14.57.

b) The separation of 5-(4-methoxyphenyl)-1,3,4-oxadiazolone-(2). 1.0 g of material was isolated from the alkaline filtrate obtained after the separation of the glyoxalidone (see above) by acidification with HCl. When this had been treated with steam, 0.17 g of material was left and this was recrystallized twice from 50% alcohol. M. p. 179-180° (0.8 g benzoic acid was isolated from the aqueous distillate).

Found %: C 56.20. H 4.26; N 14.55. $C_9H_8O_3N_2$. Calculated %: C 56.24; H 4.21; N 14.57.

4-Methoxyphenylethylenediamine dihydrochloride. 0.5 g of 5-(4-methoxyphenyl)-glyoxalidone and 25 ml HCl (1:2) were heated on the boiling water bath for 1 hour 45 minutes. The solution obtained was evaporated and the dry residue dissolved in a small quantity of water. The slight residue of unreacted glyoxalidone was filtered off and the filtrate evaporated to dryness. The substance obtained was purified by precipitation from anhydrous alcohol with absolute ether. Yield 0.5 g (80.4%).

Found %: C 45.32; H 6.60; N 11.80. $C_9H_{14}ON_2 \cdot 2HCl$. Calculated %: C 45.21; H 6.73. N 11.71.

SUMMARY

1. The synthesis of two substituted ethylenediamines has been carried out starting from the amides of acylated β-aminoacids. The latter are converted by the Hofmann reaction into the corresponding glyoxalidones, which are then decomposed to the amines by hydrochloric acid.

2. When the Hofmann reaction was carried out using the amides of β-(3,4-methylenedioxyphenyl)-β-(N-benzoylamino)-propionic and β-(4-methoxyphenyl)-β-(N-benzoylamino)-propionic acids, the products were 5-(3,4-methylenedioxyphenyl)-glyoxalidone, together with 5-(3,4-methylenedioxyphenyl)-1,3,4-oxadiazolone-(2), and 5-(4-methoxyphenyl)-glyoxalidone, together with 5-(4-methoxyphenyl)-1,3,4-oxadiazolone-(2).

3. The conditions have been worked out for breaking down 5-arylglyoxalidones, containing alkoxy groups in the benzene nucleus, into the corresponding diamines. The dihydrochlorides of 3,4-methylenedioxyphenylethylenediamine and 4-methoxyphenylethylenediamine have been prepared.

LITERATURE CITED

[1] British patent 594603; C. A. 42, 2403 (1948); British patent 604363, 604679, 604680; C. A. 43, 682 (1949); British patent 604675; C. A. 43, 822 (1949); British patent 605784; C. A. 43, 2229 (1949); British patent 606181; C. A. 43, 3471 (1949); British patent 606187; C. A. 43, 3470 (1949); British patent 606665; C. A. 43, 1437 (1949).

[2] R. Duschinsky, L. A. Doland et al, J. Am. Chem. Soc. 69, 3150 (1947).

[3] S. Kanewskaja, J. Progr. Chem. 132, 335 (1932).

[4] D. Bovet, V. Lestrange, Compt.rend.130, 1192 (1939).

[5] W. Rodionoff and E. Malewinskaja, Ber. 59, 2952 (1926).

[6] W. Rodionoff and A. Fedorova, Ber. 60, 804 (1927).

[7] W. Rodionoff amd A. Fedorova, Arch. Pharm. 266, 116 (1928).

[8] W. Rodionoff. J. Am. Chem. Soc. 51, 847 (1929).

[9] W. Rodionoff and E. Postovskaja, J. Am. Chem. Soc. 51, 841 (1929).

[10] V. M. Rodionov and N. G. Yartseva, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1952, 103 (T. p. 113) *.

[11] V. M. Rodionov and B. I. Kurtev, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1952, 113 (T. p. 123)*.

[12] V. M. Rodionov and T. S. Kiseleva, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1952, 278 (T. p. 293)*.

[13] V. M. Rodionov, Prog. Chem. 20, 273 (1951).

[14] T. Posner, Ber. 38, 2322 (1905).

[15] V. M. Rodionov and V. V. Kiseleva, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1953, 513 (T. p. 461)*.

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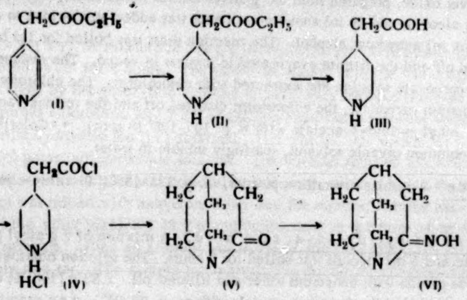
* T. p. = C. B. Translation pagination.

THE SYNTHESIS OF QUINUCLIDONE-2

L. N. Yakhontov and M. V. Rubtsov

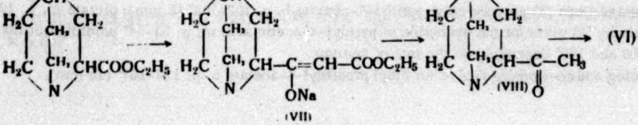
The only known oxyderivative of quinuclidine is quinuclidone-3 [1] which is the starting product for the synthesis of substances with an antispasmodic atropine-like action [2]. In the present article we describe the synthesis of another oxyderivative — quinuclidone-2 — which is a dicyclic amide. The synthesis of this compound was achieved according to the following scheme:



The starting product was ethyl pyridyl-4-acetate (I). The methods for preparing this compound described in the literature are characterized by low yields and considerable complexity [3]. It seemed to us more suitable in this case to use the Arndt-Eistert method, which enables the product (I) to be obtained from isonicotinic acid in 37 % yield. Ethyl piperidyl-4-acetate (II) was prepared by the hydrogenation of (I) in the presence of platinum catalyst prepared according to Adams. This method for the preparation of (II) is much simpler than the multistage synthesis carried out by Prelog starting from γ-pyrone [4].

Hydrolysis of (II) yielded the hydrochloride of piperidyl-4-acetic acid (III), which was converted into the corresponding chloride (IV) using thionyl chloride. The compound (IV) was converted by reaction with ignited potassium carbonate in anhydrous chloroform into quinuclidone-2 (V) — an oily substance which with hydroxylamine formed the crystalline oxime (VI).

The oxime of quinuclidone-2 (VI) was also obtained from ethyl quinuclidine-2-carboxylate by the following scheme:



Ethyl quinuclidine-2-carboxylate was condensed with ethyl acetate in the presence of sodium ethoxide. The sodium derivative of the enol form of ethyl β-(quinuclidyl-2)-β-ketopropionate (VII) was subjected to ketonic decomposition with the formation of 2-acetylquinuclidine (VIII). When 2-acetyl-quinuclidine was treated with isoamyl nitrite in the presence of sodium ethoxide [5], the product was the oxime of quinuclidone-2 (VI), identical with the oxime of quinuclidone-2 synthesized from ethyl pyridyl-4-acetate. The hydrolysis of (VI) by boiling with hydrochloric acid was accompanied by rupture of the quinuclidine ring with the formation of the hydrochloride of piperidyl-4-acetic acid (III).

EXPERIMENTAL

Ethyl pyridyl-4-acetate (I). A mixture of 6.1 g isonicotinic acid and 60 ml purified thionyl chloride was heated for 30 minutes on a water bath at 50-55°. The solution obtained was evaporated in vacuo and the traces of thionyl chloride removed by the twice repeated addition of anhydrous benzene followed by vacuum distillation. The isonicotinyl chloride hydrochloride was added with stirring to a solution of 8 g diazomethane in 100 ml anhydrous ether. The mixture was left for 48 hours at 17-20° and then evaporated in vacuo. 5.7 g diazomethyl pyridyl-4 ketone was obtained. Picrate: yellow crystals (from alcohol), m. p. 242°. *

A mixture of silver oxide, prepared from 0.3 g silver nitrate immediately before the experiment and washed with anhydrous alcohol, and 10 ml anhydrous alcohol was added portionwise to a solution of 3.4 g of the diazoketone in 50 ml anhydrous alcohol. The reaction mass was boiled for 1.5 hours, after which the precipitate was filtered off and the filtrate evaporated to dryness in vacuo. The residue was treated with 20 ml of 15 % sodium carbonate solution and extracted with chloroform. The chloroform extracts were dried with ignited potassium carbonate, the chloroform distilled off and the residue vacuum distilled. This yielded 1.7 g (37%) of ethyl pyridyl-4-acetate with b. p. 107-108° (3 mm). ** Colorless oily substance, readily soluble in the common organic solvents, sparingly soluble in water.

Hydrochloride – white crystalline powder, m. p. 135-136°. Picrate – yellow crystals, m. p. 122-123°.

The hydrazide of pyridyl-4-acetic acid. A mixture of 2 g ethyl pyridyl-4- acetate, 1.2 g hydrazine hydrate and 5 ml alcohol was boiled for 5 hours. The solution obtained was evaporated in vacuo. The residue was ground with anhydrous ether and filtered off. 1.83 g (100 %) of the hydrazide of pyridyl-4-acetic acid was obtained. Colorless crystals with m. p. 90-91°, *** readily soluble in water, acetone, chloroform, alcohol, benzene and toluene, sparingly soluble in ether.

Found %: C 55.22; H 5.94; N 27.61. $C_7H_9ON_3$. Calculated %: C 55.63; H 5.96; N 27.81.

Ethyl piperidyl-4-acetate (II). 6.3. g ethyl pyridyl-4-acetate hydrochloride, 50 ml anhydrous alcohol and 0.6 g platinum catalyst, prepared by Adams method, were hydrogenated at 17-20° under a pressure of 40-50 cm of water. The hydrogenation was completed in 24 hours. The catalyst was filtered off and the filtrate evaporated in vacuo. This yielded 6.48 g (100%) of ethyl piperidyl-4-acetate hydrochloride in the form of a white crystalline powder.

2.7 g of the hydrochloride was dissolved in water and treated with 50% potassium carbonate solution. The base which separated was extracted with ether. The ether layer was dried with potassium carbonate, the ether distilled off and the residue vacuum distilled, b. p. 125-127° (15 mm). **** 1.8 g of ethyl piperidyl-4-acetate was obtained. Colorless oily substance, readily soluble in the common organic solvents, less readily in water.

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* According to the data given by Dornow [6] the melting point of the picrate of diazomethyl pyridyl-4 ketone is 244°.

** Malan and Dean [3] give for ethyl pyridyl-4-acetate b. p. 107-108° (3 mm); picrate m. p. 121-123°.

*** Katritzky [7] gives for the hydrazide of pyridyl-4-acetic acid m. p. 51-54° pointing out that it varies between 50 and 120° depending on the rate of heating.

**** Prelog and co-workers [4] give for ethyl piperidyl-4-acetate b. p. 123-127° (15 mm).

Found %: C 63.28; H 10.03; N 7.96, 8.20. $C_9H_{17}O_2N$. Calculated %: C 63.16; H 9.94; N 8.18.

The hydrazide of piperidyl-4-acetic acid – colorless hygroscopic crystals, readily soluble in water and alcohol, sparingly soluble in ether, acetone and chloroform. M. p. 107-108.5°.

Dihydrochloride – colorless crystals, soluble in water and methanol, insoluble in ethyl alcohol and acetone. M. P. 227-228°.

Found %: C 36.67; H 7.55; N 18.25; Cl' 31.06. $C_7H_{15}ON_3 \cdot 2HCl$. Calculated %: C 36.57; H 7.39; N 18.26; Cl' 30.87.

The hydrochloride of piperidyl-4-acetic acid (III). 3.7 g of ethyl piperidyl-4-acetate hydrochloride was boiled for 5 hours with 20 ml 17% hydrochloric acid. The solution obtained was evaporated to dryness in a porcelain dish. The residue was recrystallized from a mixture of alcohol and acetone. 3 g (93.7%) of piperidyl-4-acetic acid hydrochloride was obtained. Colorless crystals, readily soluble in water and alcohol, sparingly soluble in acetone. M. p. 158-159°.

Found %: C 46.82, 47.21; H 7.69; 7.67; N 7.92; Cl' 19.63. $C_7H_{13}O_2N \cdot HCl$. Calculated %: C 46.80; H 7.80; N 7.80; Cl' 19.77.

Quinuclidone-2 (V). A mixture of 2.9 g piperidyl-4-acetic acid hydrochloride and 30 ml thionyl chloride was heated at 60° for 4 hours. The excess of thionyl chloride was distilled off in vacuo, the last traces being removed by the three-fold addition of anhydrous benzene followed by vacuum distillation. 50 ml anhydrous chloroform and 7.2 g of ignited potassium carbonate were added to the piperidyl-4-acetyl chloride hydrochloride (IV) obtained. The mixture was shaken for 2 hours and then treated with 30 ml of 30% potassium carbonate solution. The aqueous solution was extracted several times with chloroform. The chloroform extract was dried with potassium carbonate and the chloroform distilled off. The residue (2.15 g) was mixed with anhydrous ether and the solution filtered from the undissolved fraction. Evaporation of the ether yielded 1.49 g of quinuclidone-2 in the form of an oily material soluble in the common organic solvents. When an attempt was made to distil the substance in vacuo at 0.3 mm, it was converted completely to a tar. The sample for analysis was dried over phosphorus pentoxide in vacuo (at 100°) for 8 hours.

Found %: N 11.61. $C_7H_{11}ON$. Calculated %: N 11.20.

Quinuclidone-2 oxime (VI). A solution of 0.09 g quinuclidone-2, 0.05 g hydroxylamine hydrochloride and 0.06 g sodium acetate in 10 ml water was boiled for 2 hours, then evaporated to dryness and the residue extracted with anhydrous alcohol. The alcoholic solution was evaporated in vacuo and the crystals obtained — quinuclidone-2 oxime — were washed with ether. M. p. 171-172°. A mixture with quinuclidone-2 oxime prepared from 2-acetylquinuclidine melted at 171-172°.

The condensation of ethyl quinuclidine-2-carboxylate with ethyl acetate. A mixture of 1.3 [illegible]uinuclidine-2-carboxylate and 1.2 g ethyl acetate was added dropwise with stirring over a period of 50 minutes to sodium ethoxide prepared by the reaction of 0.23 g sodium with 2 ml anhydrous alcohol. Stirring was continued for a further 4 hours at room temperature and then for 10 hours with the mixture gently boiling. When 25 ml water was added to the reaction mass, a precipitate separated. The precipitate was filtered off, washed with water and dried in a vacuum desiccator 0.6 g of the sodium derivative of the enol form of ethyl β-(quinuclidyl-2)-β-ketopropionate (VII) was obtained in the form of colorless crystals with m. p. 115-116°. The substance was insoluble in water and in the common organic solvents.

Found %: C 52.23, 52.41; H 7.17, 7.24; N 5.44, 5.64. $C_{12}H_{18}O_3NNa$. Calculated %: C 52.30; H 7.28; N 5.66.

The aqueous filtrate was treated with ether to extract the ethyl quinuclidine-2-carboxylate and then boiled with hydrochloric acid; 0.3 g of 2-acetylquinuclidine was obtained from the reaction mass.

2-Acetylquinuclidine (VIII). a) A solution of the sodium derivative of the enol form of ethyl β-(quinuclidyl-2)-β-ketopropionate in 3 ml concentrated hydrochloric acid was boiled for 2 hours. The reaction mass was made alkaline with 50% potassium carbonate solution and extracted with ether. The ether extract was dried with potassium carbonate, the ether removed and the residue vacuum distilled. 0.15 g 2-acetylquinuclidine was obtained in the form of a colorless mobile oily substance with an aromatic odor. The substance was soluble in water and the common organic solvents. Yield 83% (calculated on VII).

Found %: C 70.07; H 9.68; N 9.11. $C_9H_{15}ON$. Calculated %: C 70.58; H 9.80; N 9.15.

Hydrochloride – very hygroscopic colorless crystals, m. p. 183-184° (in a sealed capillary).

b) A mixture of 9.2 g of ethyl quinuclidine-2-carboxylate and 9 g ethyl acetate was added dropwise with stirring over a period of 50 minutes to potassium ethoxide prepared from 3.9 g potassium and 14 ml anhydrous alcohol. Stirring was continued for a further 4 hours at room temperature and then for 10 hours with the mixture gently boiling. The mixture was cooled and 20 ml concentrated hydrochloric acid added to the reaction mass. The alcohol was distilled off and the reaction mass boiled under reflux for 2 hours. The reaction mass was then cooled, made alkaline with 50% potassium carbonate solution and extracted with ether. The ether extract was dried with potassium carbonate, the ether distilled off and the residue vacuum distilled. This yielded 4.8 g (61.3%, calculated on the ethyl quinuclidine-2-carboxylate) of 2-acetylquinuclidine, b. p. 94-95° (14 mm).

Phenylhydrazone — yellow crystals, soluble in organic solvents, insoluble in water. M. p. 84°.

Found %: C 68.77; H 8.79; N 15.81, 16.18; H_2O 6.97. $C_{15}H_{21}N_3 \cdot H_2O$. Calculated %: C 68.96; H 8.81; N 16.09; H_2O 6.89.

Quinuclidone-2 oxime (VIII). 2g of 2-acetylquinuclidine was added to a solution of sodium ethoxide prepared by the reaction of 0.3 g sodium with 10 ml anhydrous alcohol. The reaction mass was cooled to -5° treated with 3.4 g isoamyl nitrite and stirred for 2 hours at -5°. The pale yellow solution obtained was then made alkaline with 30 ml of 10% caustic potash solution and extracted with ether. The aqueous alkaline layer was treated with carbon dioxide until no longer alkaline to phenolphthalein. This separated the free oxime from the potassium derivative of the quinuclidone-2 oxime and this was extracted repeatedly with ether. The ether extract was dried with sodium sulfate and the ether distilled off. 1.4 g (76%) of quinuclidone-2 oxime was obtained. Colorless crystals, readily soluble in water, chloroform, alcohol and acetone, sparingly in ether and benzene. M. p. 171-172°.

Found %: C 60.04, 59.83; H 8.51, 8.56; N 20.01. $C_7H_{12}ON_2$. Calculated %: C 60.00; H 8.57; N 20.00.

The hydrolysis of quinuclidone-2 oxime. 0.8 g of quinuclidone-2 oxime was boiled for 3 hours with 8 ml 17% hydrochloric acid. The solution obtained was treated with 0.5 g sodium nitrite to decompose the hydroxylamine, decolorized with charcoal and evaporated to dryness. Piperidyl-4-acetic acid hydrochloride was extracted from the sodium chloride mixture with anhydrous alcohol. The alcohol was distilled off in vacuo. 0.9 g (87.5%) of piperidyl-4-acetic acid hydrochloride was obtained. Colorless crystals, m. p. 158-159°. The substance was identical with the piperidyl-4-acetic acid hydrochloride obtained by the hydrolysis of ethyl piperidyl-4-acetate.

SUMMARY

The synthesis of quinuclidone-2 has been carried out.

LITERATURE CITED

[1] G. R. Clemo and T. P. Metcalfe, J. Chem. Soc. 1937, 1989.

[2] L. O. Randall and W. M. Benson, J. pharm. exp. theor. 104, 3, 284 (1952); L. H. Sternbach and S. Kaiser, J. Am. Chem. Soc. 74, 2215, 2219 (1952); 75, 6068 (1953); British patent 694067 of July 15, 1953; C. A. 48, 11498 (1954); Swiss pat. 295534 of Mar. 1, 1954; J. Russ. Chem. Soc. 1955, 13, 400; U. S. patent 268067 of Nov. 3, 1953) C. A. 49, 1823 (1955).

[3] R. L. Malan and P. M. Dean, J. Am. Chem. Soc. 69, 1797 (1947).

[4] V. Prelog, Ann. 532, 69 (1937).

[5] P. Rabe, Ber. 41, 68 (1908).

[6] A. Dornow, Ber. 73, 185 (1940).

[7] A. R. Katritzky, J. Chem. Soc. 1954, 4038.

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S. Ordzhonikidze All-Union Chemical and
Pharmaceutical Scientific Research Institute

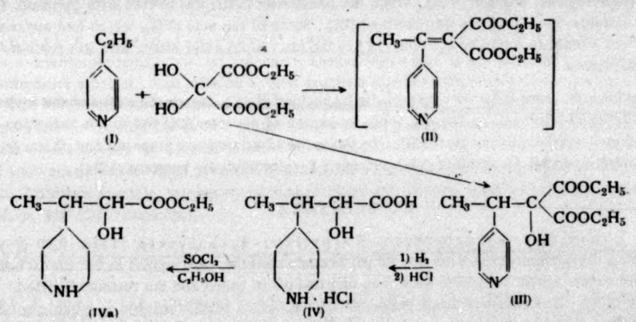
THE SYNTHESIS OF 3-METHYLQUINUCLIDINE-2-CARBOXYLIC ACID

E. E. Mikhlina and M. V. Rubtsov

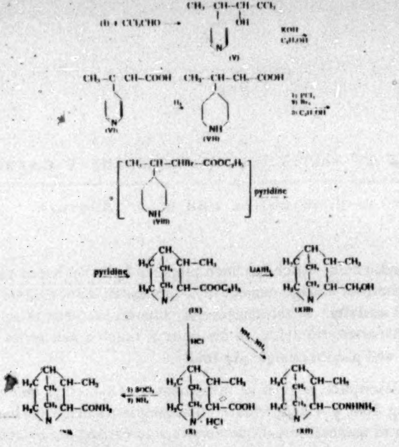
Quinuclidine-2-carboxylic acid, which has been prepared by a number of authors [1-3], is the starting material for the synthesis of a large number of 2-substituted quinuclidines [4,5], of which several show a high pharmacological activity. In this connection, interest has been attached to the previously unknown alkylquinuclidine-2-carboxylic acids, on the basis of which a new series of disubstituted quinuclidine derivatives may be prepared and pharmacologically studied.

In the present work a description is given of the synthesis of 3-methyl quinuclidine-2-carboxylic acid carried out by us starting from γ-ethylpyridine. The simplest scheme for the synthesis of this acid, by analogy with the synthesis of quinuclidine-2-carboxylic acid carried out by one of us earlier [2], appeared to be the condensation of γ-ethylpyridine (I) with dihydroxymalonic ester and subsequent conversion of the 1,1-dicarbethoxy-2-(pyridyl-4')-propene-1 (II) into 3-methylquinuclidine-2-carboxylic acid.

When (I) was condensed with dihydroxymalonic ester, however, the product obtained was not compound (II) but ethyl α-hydroxy-α-carbethoxy-β-(pyridyl-4)-butyrate (III). The reduction of the diether (III) in the presence of platinum oxide and subsequent hydrolysis and decarboxylation led to α-hydroxy-β-(piperidyl-4)-butyric acid (IV). To convert this last compound into 3-methylquinuclidine-2-carboxylic acid it was necessary to replace the α-hydroxy group in the acid (IV) by a halogen atom. With this aim the acid (IV) was treated with thionyl chloride. It turned out that at 60-65° only the chloride of the acid was formed, while increase of the temperature to 70-75° brought about considerable tar formation, and in these conditions also no replacement of the α-hydroxy group by chlorine was observed. The latter point was confirmed by the fact that when the reaction mass was treated with alcohol the only product obtained was ethyl α-hydroxy-β-(piperidyl-4)-butyrate (IVa), identical with the ester obtained by the esterification of the acid (IV) with an alcoholic solution of hydrogen chloride. The data given provide evidence that the α-hydroxy group in the acid (IV) has a low mobility, as a result of which the use of the acid (IV) for the synthesis of 3-methylquinuclidine-2-carboxylic acid proved to be impossible.



3-Methylquinuclidine-2-carboxylic acid was prepared according to the following scheme:



γ-Ethylpyridine (I) was condensed with chloral in the presence of piperidinium acetate. The 2-(pyridyl-4')-3-hydroxy-4,4,4-trichlorobutane (V) thus formed was treated with an alcoholic solution of caustic potash, as a result of which β-methyl-β-(pyridyl-4)-acrylic acid (VI) was obtained. The latter was reduced to β-(piperidyl-4)-butyric acid (VII) in hydrochloric acid solution in the presence of platinum catalyst (according to Adams) at room temperature. The acid (VII) was treated with phosphorus trichloride to give the chloride, which on treatment with bromine and then with ethyl alcohol was converted to ethyl α-bromo-β-(piperidyl-4)-butyrate (VIII). When the bromoester (VIII) was heated with pyridine, ethyl 3-methylquinuclidine-2-carboxylate was obtained (IX). Some of the acid (VII), which had not reacted with the bromine, was present in traces in the ester (IX) in the form of its ethyl ester, and was removed as the N-benzoyl derivative.

Starting from the ester (IX), we prepared the hydrochloride (X), the amide (XI) and the hydrazide (XII) of 3-methylquinuclidine-2-carboxylic acid. Reduction of the ester (IX) led to the formation of 2-hydroxymethyl-3-methylquinuclidine (XIII). In the course of the work we prepared and characterized ethyl β-methyl-β-(pyridyl-4)-acrylate (VIa) and ethyl β-(piperidyl-4)- butyrate (VIIa).

EXPERIMENTAL

Ethyl α-hydroxy-α-carbethoxy-β-(pyridyl-4)-butyrate (III). 9.73 g γ-ethylpyridine, 17.45 g dihydroxymalonic ester and 48 ml acetic anhydride were heated at 90° for 10 hours. The acetic acid and excess acetic anhydride were then distilled off in vacuo and the residue distilled. B. P. 160-162° (0.45 mm). The substance was a yellowish viscous liquid, readily soluble in organic solvents, insoluble in water. Yield 16.7 g (66%).

Found %: C 59.52; H 6.71. $C_{14}H_{19}O_5N$. Calculated %: C 59.78; H 6.76.

α-Hydroxy-β-(piperidyl-4)-butyric acid (IV). 4.5 ml 20% alcoholic solution of hydrogen chloride and 0.3 g platinum oxide catalyst (according to Adams) were added to a solution of 6.7 g ethyl α-hydroxy-α-carbethoxy-β-(pyridyl-4)-butyrate in 65 ml anhydrous alcohol. The reaction mass was shaken up with hydrogen at room temperature. When the required amount of hydrogen had been absorbed, the platinum residue was filtered off, the alcohol distilled off in vacuo and the residue boiled for 30 hours with 60 ml concentrated hydrochloric acid. The hydrochloric acid solution was decolorized with charcoal and evaporated on a water bath until crystallization commenced. The evaporated mass was diluted with acetone and the α-hydroxy-β-(piperidyl-4)-butyric acid hydrochloride was filtered off. Colorless crystals, readily soluble in water and hot alcohol, sparingly soluble in cold alcohol, insoluble in acetone and ether. M. p. 198-201°. Yield 3.2 g (52.3%).

Found %: C 48.25; H 8.04; N 6.10; Cl 15.77. $C_9H_{17}O_3N \cdot HCl$. Calculated %: C 48.32; H 8.04; N 6.26; Cl 15.88.

Ethyl α-hydroxy-β-(piperidyl-4)-butyrate. 0.5 g α-hydroxy-β-(piperidyl-4)-butyric acid hydrochloride was boiled for 4 hours with 5 ml of a 7% alcoholic solution of hydrogen chloride. The alcohol was distilled off in vacuo, the residue treated with 5 ml 50% potassium carbonate solution and extracted with ether. The ether solution was dried with potassium carbonate, the ether removed and the residue vacuum distilled. B. p. 125-128° (0.2 mm), n_D^{18} 1.4878.

Colorless viscous liquid, readily soluble in organic solvents, sparingly soluble in water. Yield 0.4 g (79%).

Found %: C 61.22; H 9.66. $C_{11}H_{21}O_3N$. Calculated %: C 61.40; H 9.76.

2-(Pyridyl-4')-3-hydroxy-4,4,4-trichlorobutane (V). 44.18 g γ-ethylpyridine, 60.8 g chloral, 2.54 g piperidine and 1.45 g glacial acetic acid were heated at 80° (in the bath) for 16 hours. The viscous reaction mass was ground with ether, the brown precipitate which separated was removed, washed with ether and dissolved in 200 ml hot ethyl acetate. The ethyl acetate solution was decolorized with charcoal, evaporated in vacuo to 1/3 of its original volume; on cooling, 39.7 g 2-(pyridyl-4')-3-hydroxy-4,4,4-trichlorobutane was obtained. When the ethereal mother liquors were evaporated and the residue subsequently recrystallized from ethyl acetate, a further 12.2 g of the above substance was obtained. Yield 51.9 g (48%). Colorless gleaming crystals, readily soluble in acetone, alcohol and ethyl acetate, insoluble in water, ether and benzene. M. p. 138-140°.

Found %: C 42.50; H 4.10; N 5.64. $C_9H_{10}ONCl_3$. Calculated %: C 42.43; H 3.92; N 5.50.

β-Methyl-β-(pyridyl-4)-acrylic acid (VI). A solution of 20 g 2-(pyridyl-4')-3-hydroxy-4,4,4-trichlorobutane in 167 ml anhydrous alcohol was added to a solution of 28 g caustic potash in 172 ml anhydrous alcohol. The solution at first acquired a green coloration and on heating this changed to brown. The reaction mass was boiled for 2 hours, cooled to 60° and carbon dioxide passed through it at this temperature to convert the caustic potash unused in the reaction into potassium bicarbonate. The inorganic salt was removed, the alcohol solution evaporated in vacuo, the residue dissolved in 15 ml water and treated with acetic acid. After 2 hours 3.1 g (24.4 %) of β-methyl-β-(pyridyl-4)-acrylic acid was filtered off. Colorless crystals, soluble on heating in water and alcohol, insoluble in ether, benzene and acetone. M. p. 218-220° (decomp.).

Found %: C 66.78; H 5.45; N 8.68. $C_9H_9O_2N$. Calculated %: C 66.26; H 5.52; N 8.60.

Ethyl β-methyl-β-(pyridyl-4)-acrylate (VIa). 1 g β-methyl-β-(pyridyl-4)-acrylic acid and 10 ml 15% alcoholic hydrogen chloride solution were heated at the boil for 4 hours. The alcohol was distilled off in vacuo, the residue treated with 10 ml 50% potassium carbonate solution and extracted with ether. The ether solution was dried with potassium carbonate, the ether removed and the substance distilled. B. p. 145° (0.5 mm). Colorless mobile liquid, readily soluble in organic solvents, insoluble in water. Yield 0.92 g (82.5%).

Found %: C 68.66; H 6.81; N 7.13. $C_{11}H_{13}O_2N$. Calculated % : C 69.11; H 6.81; N 7.33.

β-(Piperidyl-4)-butyric acid (VII). A solution of 4.3 g β-methyl-β-(pyridyl-4)-acrylic acid in 60 ml 4% hydrochloric acid was shaken with hydrogen at room temperature in the presence of 0.2 g platinum oxide (according to Adams). When the calculated amount of hydrogen (2.65 liters) had been absorbed the platinum residue was filtered off and the hydrochloric acid distilled off in vacuo. The residue was dissolved in 10 ml anhydrous alcohol and the alcohol solution diluted with ether to turbidity. After 24 hours 4.85 g (89%) of β-(piperidyl-4)-butyric acid hydrochloride was filtered off. Colorless crystals, readily soluble in water and alcohol, insoluble in acetone, ether, benzene. M. p. 144-146°.

Found %: C 51.83; H 8.59; N 6.82; Cl 17.28. $C_9H_{17}O_2N \cdot HCl$. Calculated %: C 52.05; H 8.67; N 6.74; Cl 17.11.

Ethyl β-(piperidyl-4)-butyrate (VIIa). 1.56 g β-(piperidyl-4)-butyric acid hydrochloride and 15 ml 10% alcoholic hydrogen chloride solution were heated at the boil for 3 hours. After treatment similar to that described above the ester obtained was vacuum distilled. Yield 1.25 g (83.5%). The ester was a colorless mobile liquid, readily soluble in water and organic solvents. B.p. 90-91° (0.4 min), n_D^{18} 1.4660.

Found %: N 7.11, 6.88. $C_{11}H_{21}O_2N$. Calculated %: N 7.02.

Ethyl 3-methylquinuclidine-2-carboxylate (IX). A solution of 1.65 g phosphorus trichloride in 10 ml dry chloroformwas added over a period of 10 minutes with stirring to a suspension of 5 g β-(piperidyl-4)-butyric acid hydrochloride in 20 ml anhydrous chloroform. The reaction mass was heated at 65-70° (in the bath) for 8 hours. A solution of 4.63 g bromine in 12 ml chloroform was added at 60° over a period of 1 hour to the β-(piperidyl-4)-butyryl chloride hydrochloride obtained. Heating was continued at 60° for 20 hours, 15 ml anhydrous alcohol was then added and the solution boiled for 4 hours. The alcohol was distilled off in vacuo, the residue dissolved in 15 ml water, 15 ml 50% potassium carbonate solution added to the aqueous solution and the ethyl α-bromo-β-(piperidyl-4)-butyrate (VII) extracted with ether. The ether extract was shaken for a short time with potassium carbonate, filtered, and evaporated in vacuo. The bromide obtained was boiled for 4 hours with 50 ml pyridine, the pyridine removed in vacuo, the residue treated with 20 ml of 50% potassium carbonate solution and extracted with ether. The ether solution was dried with potassium carbonate, the ether distilled off and the residue vacuum distilled. B. p. 73-80° (0.25 mm). Yield 2.4 g.

The ethyl 3-methylquinuclidine-2-carboxylate obtained contained a small quantity of ethyl β-(piperidyl-4)-butyrate as impurity. To remove this impurity the distillate was benzoylated. 0.85 g benzoyl chloride was added with cooling to a solution of 2.4 g of the distillate in 25 ml pyridine. The reaction mass was stirred for 3 hours. The pyridine was then distilled off in vacuo, the residue dissolved in 12 ml water, acidified with conc. hydrochloric acid and extracted with ether. The hydrochloric acid solution was treated with 20 ml 50% potassium carbonate solution and extracted with ether. The ether solution obtained on extraction of the alkaline solution was dried with potassium carbonate, the ether removed and the substance vacuum distilled. B. p. 112° (6 mm), 75-76° (0.25 mm). Yield 1.7 g (35.8%, calculated on the β-(piperidyl-4)-butyric acid hydrochloride taken for the reaction). Colorless mobile liquid, readily soluble in water and organic solvents.

Found %: N 7.15, 6.98. $C_{11}H_{19}O_2N$. Calculated %: N 7.10.

3-Methylquinuclidine-2-carboxylic acid hydrochloride (X). 0.55 g ethyl 3-methylquinuclidine-2-carboxylate (IX) and 6 ml 17% HCl were heated at the boil for 5 hours. 3 ml water was added to the reaction mass, the solution decolorized with charcoal and evaporated in vacuo until crystallization commenced. 10 ml acetone was then added and the crystals filtered off. Yield 0.5 g (87.5%). Colorless crystals, readily soluble in water and hot alcohol, insoluble in ether, acetone and chloroform. M. p. 292° (with decomp.).

Found %: C 52.65, 52.73; H 8.22, 8.07; N 6.70, 6.83; Cl 17.49. $C_9H_{15}O_2N \cdot HCl$.
Calculated %: C 52.55; H 7.78; N 6.80; Cl 17.28.

The amide of 3-methylquinuclidine-2-carboxylic acid (XI). 0.45 g 3-methylquinuclidine-2-carboxylic acid hydrochloride (X) and 4.5 ml thionyl chloride were heated at 70-72° for 8 hours. The excess thionyl chloride was distilled off in vacuo, 10 ml anhydrous benzene added and distilled off in vacuo (twice). The crystalline chloride of 3-methylquinuclidine - 2-carboxylic acid hydrochloride obtained was suspended in 25 ml absolute ether and the suspension saturated with ammonia with cooling. The reaction mass was treated with 15 ml 50% potassium carbonate solution, the ether layer separated and the alkaline solution extracted with chloroform. The combined chloroform and ether extracts were dried with potassium carbonate. When the solvents were removed, 0.3 g (81.5%) of the amide with m. p. 118-122° was obtained. M. p. 127.5-128.5° after two recrystallizations from ligroin (80-120°). Colorless crystals, readily soluble in water and organic solvents.

Found %: C 64.72; H 9.45; N 16.31. $C_9H_{16}ON_2$. Calculated %: C 64.32; H 9.53; N 16.65.

The hydrazide of 3-methylquinuclidine-2-carboxylic acid (XII). 0.25 g ethyl 3-methylquinuclidine-2-carboxylate (IX), 0.5 ml hydrazine hydrate and 3 ml alcohol were heated at the boil for 5 hours. The alcohol was distilled off, and the oily residue crystallized on standing in a vacuum-desiccator. 0.2 g (86.2%) of colorless crystals was obtained, readily soluble in water, alcohol, chloroform and acetone, insoluble in ether and petroleum ether. M. p. 77-82°.

Found %: N 23.21. $C_9H_{17}ON_3$. Calculated %: N 22.95.

Picrate — yellow crystals, soluble in acetone, alcohol, insoluble in water, ether. M. p. 175-177° (from alcohol).

Found %: C 43.59; H 5.24; N 20.23. $C_9H_{17}ON_3 \cdot C_6H_3O_7N_3$. Calculated %: C 43.70; H 4.85; N 20.38.

3-Methyl-2-hydroxymethylquinuclidine (XIII). 0.32 g lithium aluminum hydride was added to a solution of 0.7 g ethyl 3-methylquinuclidine-2-carboxylate (IX) in 30 ml absolute ether, and the reaction mass heated with stirring and the ether gently boiling for 2 hours. 0.7 ml water was added to the cooled mixture, and the hydroxides of lithium and aluminum filtered off and carefully washed with ether. The ether was removed and the substance distilled. B. p. 78° (0.2 mm). 0.55 g (77.3%) of colorless mobile liquid was obtained readily soluble in water and organic solvents, n_D^{20} 1.4992.

Found %: N 8.72. $C_9H_{17}ON$. Calculated %: N 9.04.

SUMMARY

A description is given of the synthesis of 3-methylquinuclidine-2-carboxylic acid and certain of its derivatives, starting from γ-ethylpyridine via 2-(pyridyl-4')-3-hydroxy-4,4,4-trichlorobutane, β-methyl-β-(pyridyl-4)-acrylic acid, β-(piperidyl-4)-butyric acid and ethyl α-bromo-β-(piperidyl-4)-butyrate.

LITERATURE CITED

[1] V Prelog and E. Cercovnikov, Ann. 532,83 (1937).

[2] M. V. Rubtsov and M. I. Dorokhova, J. Gen. Chem. 23, 706 (1953).*

[3] E. Renk and C. Grob, Helv. Chim. Acta 37, 2119 (1954).

[4] M. V. Rubtsov, E. S. Nikitskaya, E. E. Mikhlina, A. D. Yanina and V. Ya. Furshtatova, J. Gen. Chem. 23, 1555 (1953).*

[5] M. V. Rubtsov and E. S Nikitskaya, J. Gen. Chem. 24, 1659 (1954).

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S. Ordzhonikidze All-Union Chemical and
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* Original Russian pagination. See C. B. translation.

[illegible]

Found %: C 69.70 [illegible]

[illegible]

LITERATURE CITED

[1] V. [illegible]

[illegible]

[6] M. V. Rubtsov and E. S. Nikitskaya, J. [illegible]

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TETRALIN HYDROPEROXIDE. THE PREPARATION OF CERTAIN ac-α-DERIVATIVES OF TETRALIN

I. I. Chizhevskaya and Z. B. Idelchik

The present work is an attempt to use tetralin hydroperoxide as the starting compound of a series of ac-α-derivatives for the most part not described in the literature, whose preparation is difficult using existing synthetic organic chemical methods.

The method proposed for the preparation of tetralin hydroperoxide was the autoxidation of tetralin with molecular oxygen in the presence of the stearates of manganese or cobalt, which have been successfully used as initiators for the autoxidation of hydrocarbons, in work carried out in the Academy of Sciences of the Byelorussian SSR under the direction of B. V. Erofeev [1].

Works on the autoxidation of tetralin occupy an important place among the large number of works devoted to the autoxidation of hydrocarbons.

Tetralin hydroperoxide was first prepared by Hock and Susemihl [2] by the oxidation of tetralin with atmospheric oxygen. The authors of this work established the structure of the hydroperoxide obtained and studied its properties.

In later works on the study of the autoxidation of tetralin, the kinetics of the autoxidation [3] and the reaction mechanism [4] have been studied, while the products of hydroperoxide decomposition [3,5] and also side products of the oxidation, accompanying the tetralin hydroperoxide [6], have been examined.

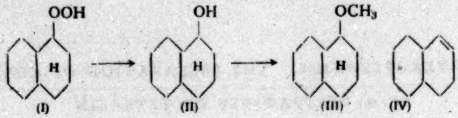
The autoxidation of tetralin in the presence of the salts of metals with organic acids has been the subject of works by K. Ivanov and co-workers [7] and by Robertson and Waters [8]. The authors of these works showed that the naphthenates of iron and manganese, while acting as exceptionally active accelerators of the autoxidation of tetralin, intensify the decomposition process of the hydroperoxides formed.

The are no data in the literature on the autoxidation of tetralin in the presence of the stearates of manganese and cobalt.

Our experiments on the autoxidation of tetralin in the presence of stearates of manganese and cobalt, taken in concentrations from 0.01 to 0.1%, have shown that these compounds considerably accelerate the process of autoxidation of tetralin. Thus, for example, in the autoxidation of tetralin in the presence of 0.01% manganese stearate at 70° with an oxygen rate of 25-30 ml/minute for 12-16 hours, the hydroperoxide content in the oxidized tetralin reaches 200-220 mg/g, whereas in the oxidation of pure tetralin at 75-85° with an oxygen rate of 80-100 ml/minute, the same hydroperoxide content is reached after 60-66 hours. The yield of tetralin hydroperoxide in the autoxidation of tetralin in the presence of 0.01% manganese stearate equals 78-86% calculated on the original tetralin. The tetralin hydroperoxide obtained is slightly contaminated by side-products of the oxidation, and on cooling the oxidized fraction of the tetralin to a temperature of +5° it separates in the form of white needle-like crystals, which after being washed twice with petroleum ether have a melting point corresponding to that given in the literature for tetralin hydroperoxide [2,3].

The autoxidation of tetralin in the presence of 0. 1% manganese stearate and also in the presence of cobalt stearate (0.1, 0.01%), leads to lower yields of tetralin hydroperoxide (60-70%), and the hydroperoxide obtained is strongly contaminated by viscous side-products of the autoxidation, as a result of which it cannot be isolated in a crystalline form.

The tetralin hydroperoxide (I) obtained was reduced by sodium sulfite to the corresponding alcohol ac-α-tetralol(III) [9].



(I) (II) (III) (IV)

When the α-tetralol was heated with methyl alcohol in the presence of a few drops of concentrated sulfuric acid the product was the ac-α-methoxytetralin (III).

A notice is given in the literature on the preparation of ac-α-methoxy- β-bromotetralin by the action of methyl alcohol in 1,2-dibromotetralin [10], but there are no notices in the literature on the preparation of ac-α-methoxytetralin.

It should be noted that when the etherification of ac-α-tetralol was carried out at temperatures above 60° we obtained, together with the α-methoxytetralin, a considerable amount of 1,2-dihydronaphthalene (IV) — the product of dehydration of ac-α-tetralol, which takes place evidently at the same time as the etherification process.

In experiments on the preparation of ac-α-chlorotetralin we observed that the reaction took a similar course. When ac-α-tetralol was heated with concentrated hydrochloric acid, a considerable amount of 1,2-dihydronaphthalene (IV) was formed with the ac-α-chlorotetralin.

There is a notice in the literature on the ability of ac-α-tetralol to undergo dehydration, which takes place quantitatively when the alcohol is heated with caustic potash to a temperature of 200-210° [2], and this ability to undergo dehydration is evidently even more strongly pronounced when the ac-α-tetralol is heated in the presence of mineral acids, but there are no notices on this point in the literature.

ac-α-Chlorotetralin was prepared by heating ac-α-tetralol with hydrochloric acid.

In contrast to the ac-β-chlorotetralin described in the literature [11], which decomposes with the liberation of hydrogen chloride when heated in vacuo to a temperature of 50°, ac-α-chlorotetralin is distilled in vacuo without decomposition.

ac-α-Chlorotetralin was used by us for the synthesis of ac-α-acetoxytetralin and ac-α-diethylaminotetralin.

Our experiments have shown that the mobility of the chlorine atom situated in the α-position of the tetralin hydroaromatic nucleus is considerably lower than the halide mobility characteristic of alicyclic hydrocarbons. Thus, for example, an attempt to replace the chlorine atom by the nitro group by the action of nitric acid on ac-α-chlorotetralin at a temperature of 12-15° [12] was unsuccessful: the original ac-α-chlorotetralin was recovered unchanged from the reaction.

ac-α-Acetoxytetralin was prepared only by heating ac-α-chlorotetralin with silver acetate in glacial acetic acid, and also by the etherification of ac-α-tetralol with acetic anhydride in pyridine.

To prepare ac-α-diethylaminotetralin from ac-α-chlorotetralin, it was necessary to heat the latter with diethylamine under pressure, at a temperature of 110-120°. When the starting materials were heated at 60-70° the alkylation did not take place.

EXPERIMENTAL

The tetralin, after being dried over anhydrous MgSO$_4$ and distilled in vacuo from metallic sodium, had the following constants:

B. p. 67–72° (3.5 mm), n_D^{20} 1.5475, d_4^{20} 0.9705, MR_D 43.17; Calc. 42.58.

The manganese stearate was prepared from sodium stearate and manganese nitrate [13].

Found %: Mn 7.34. $Mn(C_{17}H_{35}COO)_2$. Calculated %: Mn 8.83.

The autoxidation of tetralin in the presence of 0.01% manganese stearate. 100 g tetralin and 0.013 g manganese stearate were placed in a three-necked glass flask fitted with stirring propellor. The contents of the flask were heated to 70° after which the mechanical stirrer was switched off and oxygen (purified by passing through ascarite, H_2SO_4 and $CaCl_2$) was passed through using a bubbler consisting of a glass tube reaching to the foot of the flask. The rate of passage of the oxygen was 25-30 ml/minute. Test samples of the reaction mass were removed periodically from the reaction flask and analysed for tetralin hydroperoxide content.

The tetralin hydroperoxide content was determined using an iodometric method [13].

The sample of the reaction mass weighing approximately 0.02 g was placed in an Erlenmeyer flask of 100 ml capacity fitted with a ground glass stopper, after which 5 ml 97% acetic acid and 5 ml 10% potassium iodide were added. The mixture was left in the dark at 18-20°. After 1 hour the liberated iodine was titrated with 0.1 N sodium thiosulfate solution from a microburet. A blank experiment was carried out simultaneously.

1 ml 0.1 N sodium thiosulfate solution corresponds to 8.2 mg tetralin hydroperoxide in 1 g of the reaction mass.

When the tetralin hydroperoxide content in 1 g of the reaction mass had reached 200-220 mg, the oxidation was stopped. The unreacted tetralin was distilled off on the water bath at a temperature of 65-70° (2 mm). The residue in the distillation flask (23.5 g) was placed in a freezing mixture. After some time the tetralin hydroperoxide was seen to crystallize. The crystals were washed twice on a filter with petroleum ether; 18.7 g (79.5%) of pure tetralin hydroperoxide was obtained, m. p. 55°.

Found %: C 73.31; H 7.74. $C_{10}H_{12}O_2$. Calculated %: C 73.17; H 7.31.

The reduction of tetralin hydroperoxide. 30 g sodium sulfite was gradually added portionwise in the form of a 20% solution to 28 g of tetralin hydroperoxide dissolved in 40 ml methyl alcohol. The reduction was carried out in a vessel placed in a vigorous mechanical shaker. The addition of the sodium sulfite was accompanied by a powerful evolution of heat by the contents of the flask, so that the latter was periodically cooled with a stream of cold water. After 5 hours shaking at room temperature the reaction product, which had separated on the surface in the form of an oil with a pinkish color, was extracted with ether. The ether extracts were dried over $MgSO_4$ and vacuum distilled.

24 g (95%, calculated on the tetralin hydroperoxide) of ac-α-tetralol was obtained in the form of a thick colorless glycerol-like liquid with a sharp unpleasant odor.

B. p. 107° (2 mm), n_D^{20} 1.5673, d_4^{20} 1.0996, MR_D 43.99; Calc. 44.10.

Found %: C 81.58; H 7.86; OH 10.29. $C_{10}H_{12}O$. Calculated %: C 81.08; H 8.10; OH 11.49.

ac-α-Tetralyl α-naphthylurethan was prepared from 0.5 g ac-α-tetralol and 0.5 g α-naphthyl isocyanate at room temperature. After 18 hours a white crystalline precipitate was obtained, which after two recrystallizations from dilute methyl alcohol melted at 145-145.5°.

Found %: C 79.70; H 6.06; N 4.67. $C_{21}H_{19}O_2N$. Calculated %: C 79.53; H 5.99; N 4.42.

The preparation of ac-α-methoxytetralin. 5.2 g ac-α-tetralol mixed with 15 ml anhydrous methyl alcohol was heated at 60° in the presence of one drop of concentrated sulfuric acid for 9 hours. The reaction mass was poured into water and the oil which separated was extracted with ether.

The ether extracts were dried over anhydrous $MgSO_4$ and vacuum distilled.

4.4 g (78 %, calculated on the ac-α-tetralol) of substance was isolated. Highly mobile liquid with a pleasant fruity odor.

B. p. 90-92.5° (2.5 mm), n_D^{20} 1.5430, d_4^{20} 1.0343, MR_D 49.36; calc. 48.84.

Found %: C 81.36; H 8.70; OCH_3 18.42. $C_{11}H_{14}O$. Calculated %: C 81.48; H 8.71; OCH_3 19.13.

The preparation of 1,2-dihydronaphthalene. A mixture of 5 g of ac-α-tetralol and 25 ml methyl alcohol, to which had been added 0.3 g concentrated sulfuric acid, was heated on a boiling water bath for 7 hours. The solution was cooled, the sulfuric acid neutralized with barium carbonate, the precipitate which formed filtered off and the filtrate vacuum distilled. 2.5g of substance was obtained.

B. p. 77° (5 mm), n_D^{20} 1.5832, d_4^{20} 1.0016, MR_D 43.40; calc. 42.11.

Found %: C 92.0 ; H 8.08. $C_{10}H_{10}$. Calculated %: C 92.3; H 7.69.

Contains no active hydrogen (Chugaev-Tserevitinov method).

0.3 g of the substance obtained was mixed with 20 ml chloroform and cooled (ice + salt) to a temperature of -2° and then brominated (0.5 g bromine in 10 ml chloroform). The chloroform was distilled off in vacuo and the residue in the distillation flask washed with water. The crystals which separated were dried in air and recrystallized from petroleum ether. The crystalline material melted at 68-69° which corresponds to 1,2-dibromotetralin [10].

The preparation of ac-α-chlorotetralin. 5 g ac-α-tetralol was heated with 50 ml hydrochloric acid (d 1.19) at 40-45° for 6 hours. The reaction mass was cooled to room temperature, poured into cold water (400 ml), and the oil which separated was extracted with ether. The ether extracts were washed with 0.5 % sodium carbonate solution and then with water until neutral to litmus after which they were dried over $MgSO_4$ and vacuum distilled. 4.4 g (77%) of a colorless mobile liquid with a sharp unpleasant odor was isolated.

B. p. 98-100° (2 mm), n_D^{20} 1.5698, d_4^{20} 1.1474, MR_D 47.68; calc. 47.44.

Found %: C 71.93; H 6.79; Cl 21.50. $C_{10}H_{11}Cl$. Calculated %: C 72.28; H 6.60; Cl 21.30.

Contains no active hydrogen (Chugaev-Tserevitinov method).

The preparation of ac-α-diethylaminotetralin. 20 g ac-α-chlorotetralin and 25 g diethylamine in two glass tubes were heated at 110-120° for 25 hours. The tubes were cooled and opened, and the crystalline material which had formed inside them (the hydrochlorides of the excess diethylamine and the amino derivative) was dissolved in water. The free base of the aminoderivative was isolated in the form of an oil from the aqueous solution when the latter was made alkaline, and the oil was extracted with ether. The ether extracts were washed repeatedly with water to remove the excess diethylamine, then dried over $MgSO_4$ and vacuum distilled. 16.6 g (68%) of ac-α-diethylaminotetralin was obtained in the form of a mobile liquid with an unpleasant odor.

B. p. 100-102° (1.5 mm), n_D^{20} 1.5382, d_4^{20} 0.9819, MR_D 65.01; calc. 64.99.

Found %: C 82.93; H 10.70; N 7.20. $C_{14}H_{21}N$. Calculated %: C 82.75; H 10.34; N 6.89.

When dry gaseous HCl was passed through an alcoholic solution of the amine, a white crystalline precipitate of the hydrochloride was obtained, rapidly deliquescing in air.

The preparation of ac-α-acetoxytetralin. a) Starting from ac-α-chlorotetralin. 3.6 g of ac-α-chlorotetralin was heated with 4 g silver acetate in 4 ml glacial acetic acid at a temperature of 60° for 6 hours. The reaction mass was cooled, poured into water, and the oil which separated was extracted with ether. The ether extract was dried over anhydrous $MgSO_4$ and vacuum distilled.

B. p. 112-114° (2.5 mm), n_D^{20} 1.5286, d_4^{20} 1.0810, MR_D 54.18; calc. 53.47.

Found %: C 75.59; H 7.49. $C_{12}H_{14}O_2$. Calculated %: C 75.79; H 7.58.

b) Starting from ac-α-tetralol. 30 g was heated with 23 g freshly distilled acetic anhydride in presence of 18 g pyridine at 60° for 6 hours. The reaction mass was cooled, poured into 2 liters of water containing 200 ml 3 N hydrochloric acid, and the oil which separated was extracted with ether. The ether extracts were washed with water, dried over $MgSO_4$ and then vacuum distilled. 24.8 g (66%) of substance was obtained.

B. p. 108-109° (1.5–2 mm), n_D^{20} 1.5290, d_4^{20} 1.0815, MR_D 54.29; calc. 53.47.

Found %: C 75.72; H 7.72. $C_{12}H_{14}O_2$. Calculated %: C 75.79; H 7.58.

The authors have to thank B. V. Erofeev for suggesting the theme for study and for creating the conditions in which it could be carried out.

SUMMARY

1. A more rapid method for preparing tetralin hydroperoxide has been worked out, involving the oxidation of tetralin with oxygen in the presence of 0.01% manganese stearate at a temperature of 70° and with a rate of passage of oxygen of 30 ml/minute.

2. It has been shown possible to synthesize ac-α-derivatives of tetralin starting from tetralin hydroperoxide; ac-α-methoxytetralin, ac-α-chlorotetralin and ac-α-diethylaminotetralin have been prepared and characterized for the first time.

3. It has been shown that when ac-α-tetralol is heated in the presence of mineral acids (H_2SO_4, HCl) to temperatures above 60-70° partial dehydration of the ac-α-tetralol takes place with the formation of 1,2-dihydronaphthalene.

LITERATURE CITED

[1] B. V. Erofeev, A. Chirko and L. Sorokina, Sci. Repts. Byelorussian State Univ., No. 20, Chem. Series, 3, 17 (1954).

[2] H. Hock and W. Susemihl, Ber. 66, 61 (1933); H. Hartmann and W. Seibert, Helv. Chim. Acta 15, 1390 (1932).

[3] S. Medvedev, A. Podyapolskaya, J. Phys. Chem. 13, 716 (1939).

[4] K. Ivanov, Intermediate Products and Intermediate Reactions in the Autoxidation of Hydrocarbons• (State Fuel Tech. Press, 1949).

[5] A. Robertson and W. Waters, J. Chem. Soc. 1948, 1574.

[6] A. Kamneva and L. Salmin, Trans. Mendeleev Chem. Tech. Inst., Moscow 18, 210 (1954); Problems in Hydrocarbon Oxidation• (Acad. Sci. USSR Press, 1954), 140.

[7] K. Ivanov, V. Savinova and E. Mikhailova, Proc. Acad. Sci. USSR 35, 41 (1939).

[8] A. Robertson and W. Waters, Trans. Far. Soc. 42, 201 (1946).

[9] J. Davies and A. White, J. Chem. Soc. 1952, 3300.

[10] German patent 335477; Frdl., 13, 328 (1921).

[11] E. Bamberger and W. Lodter, Ber. 27, 943 (1894).

[12] Guben, Organical Chemical Methods 3, 475 (1935).

[13] R. Lombard and A. Kohler, Bull. Soc. Chim. 5, 639 (1951).

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Institute of Chemistry
Academy of Sciences, Byelorussian SSR

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HETEROCYCLIC COMPOUNDS

49. SYNTHETIC PAIN-RELIEVING MATERIALS. XI. ESTERS OF 1-CARBALKOXYALKYL-2,5-DIMETHYL-4-PIPERIDOLS

I. N. Nazarov, R. I. Kruglikova and L. A. Bukhtenko

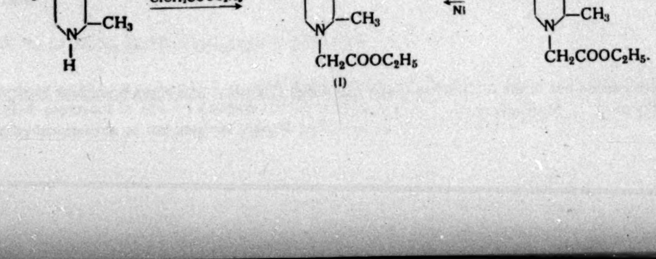
In recent years increased interest has been attached to esters of 4-piperidols with different substituents in the piperidine ring and on the nitrogen atom. As has been shown in a number of works from our laboratory [1], and by other authors [2], the esters of 4-piperidols with aromatic acids possess a high anesthetic activity, while the esters of 4-phenyl-4-piperidols and fatty acids are effective analgesics. Thus 1,2,5-trimethyl-4-phenyl-4-piperidyl propionate hydrochloride which was synthesized in our laboratory and has come into medical practice under the name "Promedol", is several times more active than morphine, is less toxic, and does not cause addiction.

With the aim of studying the influence of structure on the physiological activity of compounds we have prepared esters of 4-piperidols with carboxyl substituents on the nitrogen. These compounds may also be regarded as analogs of eucaines and of an "open cocaine" in which the ester group is situated not on the carbon atoms of the piperidine ring but in the substituent on the nitrogen. These compounds, which had previously been almost unobtainable, became readily available after a simple and convenient method had been worked out in our laboratory for the preparation of different 4-piperidols by cyclizing dienones using ammonia and primary amines [3].

We attempted to prepare 1-carbalkoxyalkyl-2,5-dimethyl-4-piperidols in two ways: 1) by reduction of the previously prepared 1-carbethoxymethyl-2,5-dimethyl-4-piperidone and 2) by introduction of the carboxylic ester residue into the 2,5-dimethyl-4-piperidol molecule.

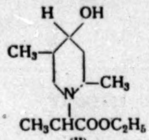
When 1-carbethoxymethyl-2,5-dimethyl-4-piperidone was hydrogenated in an autoclave under a hydrogen pressure of 125 atm in the presence of a Ni catalyst, the product was a mixture of stereoisomeric 1-carbethoxymethyl-2,5-dimethyl-4-piperidols, from which only one crystalline isomer with m. p. 95-96° (I) could be isolated. As I. N. Nazarov and co-workers [4] have recently shown, the reduction of 2,5-dimethyl-4-piperidone in different conditions leads to the formation of three stereoisomeric forms of 2,5-dimethyl-4-piperidol (α, β and γ) from the four theoretically possible.

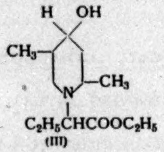
The reaction of the α-form of 2,5-dimethyl-4-piperidol with chloroacetic ester also led to the formation (in 64 % yield) of the above-mentioned isomer of 1-carbethoxymethyl-2,5-dimethyl-4-piperidol (I) with m. p. 95-96°:

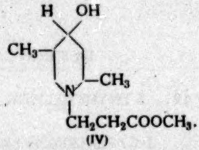


(I)

The α-isomers of 1-α-carbethoxyethyl-2,5-dimethyl-4-piperidol (II) and 1-α-carbethoxypropyl-2,5-dimethyl-4-piperidol (III) were prepared (in 62 and 54% yields) by treating the α-form of 2,5-dimethyl-4-piperidol (m. p. 97-98°) with ethyl α-bromopropionate and ethyl α-bromobutyrate respectively. The α-isomer of 1-β-carbomethoxyethyl-2,5-dimethyl-4-piperidol (IV) was prepared (in 75% yield) by the addition of methyl acrylate to the α-form of 2,5-dimethyl-4-piperidol:

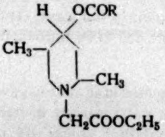

(II)

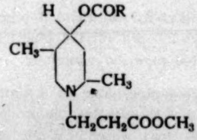

(III)

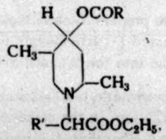

(IV)

The reaction of 2,5-dimethyl-4-piperidol with the esters of α-halogeno-substituted carboxylic and acrylic acids was carried out in the same way as the reaction of 2,5-dimethyl-4-piperidone with the same reagents [5]. The piperidols (I-IV) were esterified with acetic and propionic anhydrides and with benzoyl chloride.

To prepare the acetates, the appropriate piperidol was added to a 7-10-fold excess of acetic anhydride previously saturated with hydrogen chloride, and the mixture heated at 80-90°. When the reaction was complete, dry hydrogen chloride was again passed into the reaction mass, the excess acetic anhydride and acetic acid distilled off in vacuo and the residue treated with absolute ether. The propionates and benzoates of 1-carbalkoxyalkyl-2,5-dimethyl-4-piperidols were prepared similarly. The hydrochlorides, which are convenient for pharmacological testing and are readily soluble in water, were obtained in the esterification process and purified by recrystallization. The free bases were isolated only in those cases where the hydrochlorides were obtained in the form of an oil which crystallized with difficulty. In one case, in the preparation of 1-carbethoxymethyl-2,5-dimethyl-4-piperidyl acetate, the esterification was carried out in the presence of concentrated sulfuric acid; this reaction led to the formation of the sulfate of the acetate and this was also readily soluble in water. In this way the following esters were obtained:


(V) $R = CH_3$,
(VI) $R = C_2H_5$,
(VII) $R = C_6H_5$,


(VIII) $R = CH_3$,
(IX) $R = C_2H_5$,
(X) $R = C_6H_5$,


(XI) $R = C_6H_5$, $R' = CH_3$,
(XII) $R = C_2H_5$, $R' = CH_3$,
(XIII) $R = C_6H_5$, $R' = C_2H_5$.

Pharmacological tests showed,* that compounds (V), (VI) and (VIII) show no pain-relieving activity. When given in doses of 50 mg/kg, they do not raise the threshold of pain sensitivity. The compounds (X) and (XI) show a very weak anesthetic activity. The compound (VII) showed a considerable anesthetic activity; its effect approaches that of novocaine. A comparison of 1-carbalkoxyalkyl-2,5-dimethyl-4-piperidyl benzoates with the 1-alkyl-2,5,dimethyl-4-piperidyl benzoates previously prepared in our laboratory [1] led to the conclusion that the replacement of the alkyl substituent on the nitrogen by a carbalkoxy group leads to a lowering of the anesthetic activity of the compound.

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* The tests were carried out in the S. Ordzhonikidze All-Union Chemical and Pharmaceutical Institute in the laboratory of M. D. Mashkovsky.

EXPERIMENTAL

1-Carbethoxymethyl-2,5-dimethyl-4-piperidol (I). a)16.6 g ethyl chloroacetate was poured into a solution of 38 g of the α-isomer of 2,5-dimethyl-4-piperidol (m. p. 97-98°) [4] in 45 ml alcohol. Crystals of 2,5-dimethyl-4-piperidol hydrochloride began to separate after 30 minutes. The mixture was left for 24 hours at room temperature and then heated for 3 hours at 80-90°. The alcohol was distilled off in vacuo, the residue dissolved in 75 ml water, extracted three times with ether and dried with sodium sulfate. The product crystallized on removal of the ether. Two recrystallizations from a mixture of benzene and benzine (1:2) yielded 16.8 g (64 %) of 1-carbethoxymethyl-2,5-dimethyl-4-piperidol with m. p. 95-96°.

Found %: N 6.55, 6.69. $C_{11}H_{21}O_3N$. Calculated %: N 6.51.

The picrate, after two recrystallizations from alcohol, melted at 151-152°.

Found %: N 12.63, 12.66. $C_{17}H_{24}O_{10}N_4$. Calculated %: N 12.61.

The hydrochloride of 1-carbethoxymethyl-2,5-dimethyl-4-piperidol, after recrystallization from acetone, melted at 131-132°.

Found %: Cl 13.91. $C_{11}H_{22}O_3NCl$. Calculated %: Cl 14.11.

15.5 g of the original 2,5-dimethyl-4-piperidol was isolated from the aqueous layer by treatment with potassium carbonate and extraction with ether.

b) 27 g of 1-carbethoxymethyl-2,5-dimethyl-4-piperidol was hydrogenated in an autoclave at a hydrogen pressure of 125 atm in the presence of Raney nickel catalyst (5 g). The calculated quantity of hydrogen was absorbed. When hydrogenation was complete the catalyst was filtered off, the alcohol (introduced in washing the catalyst and autoclave) distilled off in vacuo, and the product left to crystallize. Large needle-like crystals of 1-carbethoxymethyl 2,5-dimethyl-4-piperidol (7.6 g) were formed overnight. After 2 recrystallization from a mixture of benzene and benzine (1:2) the product melted at 95-96° and gave no melting point depression with the sample prepared in experiment "a".

Found %: C 61.39; H 9.71; N 6.59, 6.58. $C_{11}H_{21}O_3N$. Calculated %: C 61.36; H 9.63; N 6.51.

The filtrate (17.5 g) remaining after removal of the crystals was vacuum distilled and had b. p. 125.5-126° (1 mm), n_D^{20} 1.4751. On prolonged standing, crystals with m. p. 95-96° slowly separated from it.

1-α-Carbethoxyethyl-2,5-dimethyl-4-piperidol (II). A mixture of 20 g 2,5-dimethyl-4-piperidol, 120 ml acetone and 13.8 g ethyl α-bromopropionate was left to stand for 24 hours at room temperature and then heated for 18 hours at 60°. The crystals of 2,5-dimethyl-4-piperidol hydrobromide which precipitated were separated, the acetone distilled off and the product vacuum distilled. 11 g (63 %) of 1-α-carbethoxyethyl-2,5-dimethyl-4-piperidol (II) was obtained in the form of a thick colorless liquid.

B. p. 129-132° (5 mm), n_D^{20} 1.4761.

Found %: N 6.30, 6.34. $C_{12}H_{23}O_3N$. Calculated %: N 6.12.

The hydrochloride of 1-α-carbethoxyethyl-2,5-dimethyl-4-piperidol melted at 169-170° (from acetone).

Found %: Cl 13.78, 13.82. $C_{12}H_{24}O_3NCl$. Calculated %: Cl 13.70.

1-α-Carbethoxypropyl-2,5-dimethyl-4-piperidol (III). A mixture of 35 g 2,5-dimethyl-4-piperidol in 150 ml acetone and 27 g ethyl α-bromobutyric acid was heated for 24 hours at 60°. The hydrobromide of the original piperidol (15.5 g) which precipitated was filtered off. The acetone solution was again heated for 12 hours at 60° during which 2 g of the hydrobromide of the original piperidol was precipitated. The acetone was distilled from the mother solution and the residue vacuum distilled. 18 g (54%) of 1-α-carbethoxypropyl-2,5-dimethyl-4-piperidol was obtained in the form of a thick colorless liquid with b. p. 138-140° (2.5 mm), n^{19}_D 1.4798.

Found %: N 6.55, 6.72. $C_{13}H_{25}O_3N$. Calculated %: N 6.49.

The hydrochloride precipitated in the form of an oil which did not crystallize well.

1-β-Carbomethoxyethyl-2,5-dimethyl-4-piperidol (IV). A solution of 23 g 2,5-dimethyl-4-piperidol in 20 g methyl acrylate was heated for 6 hours at 110-120°. The excess methyl acrylate was distilled off and the product remaining vacuum distilled. 29 g (75%) of 1-β-carbomethoxyethyl-2,5-dimethyl-4-piperidol was obtained in the form of a viscous colorless liquid which turned yellow on standing in air. B. p. 122-126° (1 mm).

n^{20}_D 1.4611, d^{20}_4 1.053, MR 58.11; calc. 57.91.

Found %: N 6.77, 6.97. $C_{11}H_{21}O_3N$ Calculated %: N 6.58.

The hydrochloride was obtained as hygroscopic white crystals with m. p. 129-132°.

The picrate melted at 153-153.5° (from alcohol).

Found %: N 12.63, 12.42. $C_{17}H_{24}O_{10}N_4$. Calculated %: N 12.60.

1-Carbethoxymethyl-2,5-dimethyl-4-piperidyl acetate (V). a) A solution of 2 g 1-carbethoxymethyl-2,5-dimethyl-4-piperidol (m. p. 95-96°) in 10 g of acetic anhydride previously saturated with dry hydrogen chloride was heated on a boiling water bath for 5 hours. The solution was cooled and dry hydrogen chloride again passed through. The excess acetic anhydride and acetic acid were distilled off in vacuo and the glassy mass which remained crystallized on treatment with ether. This was precipitated three times from alcohol with ether to yield 2.5 g (96%) of 1-carbethoxymethyl-2,5-dimethyl-4-piperidyl acetate hydrochloride with m. p. 165.5-166.5° readily soluble in water, alcohol and acetone.

Found %: N 4.88, 4.56; Cl 11.97. $C_{13}H_{24}O_4NCl$. Calculated %: N 4.77; Cl 12.10.

b) A mixture of 0.7 g 1-carbethoxymethyl-2,5-dimethyl-4-piperidol, 3.2 g acetic anhydride and 0.3 g concentrated sulfuric acid was heated for 3 hours on a boiling water bath. The crystals which precipitated were washed twice with ether. After 2 recrystallizations from aqueous (50%) alcohol, 0.62 g 1-carbethoxymethyl-2,5-dimethyl-4-piperidyl acetate sulfate with m. p. 226-227° (with tar formation) was obtained.

Found %: N 4.49, 4.65 $(C_{13}H_{23}O_4N_2)_2 \cdot H_2SO_4$. Calculated %: N 4.57.

1-Carbethoxymethyl-2,5-dimethyl-4-piperidyl propionate (VI). A solution of 6 g 1-carbethoxymethyl-2,5-dimethyl-4-piperidol in 39 g propionic anhydride previously saturated with dry hydrogen chloride was heated for 5 hours on a boiling water bath. The solution was cooled and dry hydrogen chloride again passed through. The excess propionic anhydride was distilled off in vacuo and the residue treated with ether. This was precipitated three times from alcohol with ether to yield 7.8 g of the hydrochloride of 1-carbethoxymethyl-2,5-dimethyl-piperidyl propionate (VI) with m. p. 146-147° readily soluble in water, alcohol and acetone.

Found %: N 4.42, 4.39; Cl 11.61. $C_{14}H_{26}O_4NCl$. Calculated %: N 4.55; Cl 11.54.

1-Carbethoxymethyl-2,5-dimethyl-4-piperidyl benzoate (VII). A solution of 4 g 1-carbethoxymethyl-2,5-dimethyl-4-piperidol in 13 g benzoyl chloride was heated for 4 hours on a glycerol bath at 100-105°. The excess benzoyl chloride was distilled off and the residue treated with ether. This was precipitated three times from alcohol with ether to yield 5.2 g 1-carbethoxymethyl-2,5-dimethyl-4-piperidyl benzoate hydrochloride with m. p. 166-167° readily soluble in water, alcohol and acetone.

Found %: N 4.02, 4.06; Cl 10.08. $C_{18}H_{26}O_4NCl$. Calculated %: N 3.94; Cl 9.99.

1-β-Carbomethoxyethyl-2,5-dimethyl-4-piperidyl acetate (VIII). 10 g of 1-β-carbomethoxyethyl-2,5-dimethyl-4-piperidol and 49.2 g freshly distilled acetic anhydride were taken. The acylation was carried out as described above. 7.5 g 1-β-carbomethoxyethyl-2,5-dimethyl-4-piperidyl acetate hydrochloride was obtained and after 2 recrystallizations from anhydrous alcohol this melted at 161.5-162° Readily soluble in water, alcohol and acetone.

Found %: N 4.87, 4.75; Cl 11.95. $C_{13}H_{24}O_4NCl$. Calculated %: N 4.77; Cl 12.09.

1-β-Carbomethoxyethyl-2,5-dimethyl-4-piperidyl propionate (IX). 11 g of 1-β-carbomethoxyethyl-2,5-dimethyl-4-piperidol and 33 g propionic anhydride were taken. The reaction was carried out as described above. This yielded 9.7 g of 1-β-carbomethoxyethyl-2,5-dimethyl-4-piperidyl propionate hydrochloride which melted at 131.5-132° after 2 recrystallizations from anhydrous alcohol. Readily soluble in water, alcohol and acetone.

Found %: C 54.44, 54.75; H 8.23, 8.44; Cl 11.69. $C_{14}H_{26}O_4NCl$. Calculated %: C 54.70; H 8.46; Cl 11.55.

1-β-Carbomethoxyethyl-2,5-dimethyl-4-piperidyl benzoate (X). 18 g of 1-β-carbomethoxyethyl-2,5-dimethyl-4-piperidol and 75 g benzoyl chloride were taken. The benzoylation was carried out as described above. 18.9 g of 1-β-carbomethoxyethyl-2,5-dimethyl-4-piperidyl benzoate hydrochloride with m. p. 181-181.5° (from alcohol)was obtained. Readily soluble in water, alcohol and acetone.

Found %: N 3.99, 4.45; Cl 9.85, 9.74. $C_{18}H_{26}O_4NCl$. Calculated %: N 3.94; Cl 9.99.

1-α-carbethoxyethyl-2,5-dimethyl-4-piperidyl benzoate (XI). 6.5 g of 1-α-carbethoxyethyl-2,5-dimethyl-4-piperidol and 20 g benzoyl chloride were taken. The reaction was carried out as described above. This yielded 5 g of the hydrochloride of 1-α-carbethoxyethyl-2,5-dimethyl-4-piperidyl benzoate (XI) with m. p. 193.5-194° (from alcohol). Readily soluble in water, alcohol and acetone.

Found %: C 61.86, 61.62; H 7.55, 7.74. $C_{19}H_{28}O_4NCl$. Calculated %: C 61.77; H 7.59.

1-α-Carbethoxyethyl-2,5-dimethyl-4-piperidyl propionate (XII). 2.5 g 1-α-carbethoxyethyl-2,5-dimethyl-4-piperidol and 13 g propionic anhydride were taken. The reaction was carried out as described above. Since the hydrochloride of the propionate could not be crystallized, it was converted into the free base. 1.8 g of- 1-α-carbethoxyethyl-2,5-dimethyl-4-piperidyl propionate was obtained in the form of a thick liquid with b. p. 135-137°(3.5 mm).

Found %: N 5.19, 5.28. $C_{15}H_{27}O_4N$. Calculated %: N 4.95.

1-α-Carbethoxypropyl-2,5-dimethyl-4-piperidyl benzoate (XIII). 6 g of 1-α-carbethoxypropyl-2,5-dimethyl-4-piperidol and 20 g benzoyl chloride were taken. The reaction was carried out as described above. This yielded 3 g of 1-α-carbethoxypropyl-2,5-dimethyl-4-piperidyl benzoate in the form of a viscous liquid with b. p. 185-190° (4.5 mm).

Found %: N 4.32, 4.27. $C_{20}H_{29}O_4N$. Calculated %: N 4.04.

SUMMARY

1. Three methods: a) the reduction of 1-carbalkoxyalkyl-2,5-dimethyl-4-piperidone, b) the action of esters of α-halogenosubstituted acids on 2,5-dimethyl-4-piperidol and c) the addition of acrylic esters to 2,5-dimethyl-4-piperidol, have been used to prepare 1-carbalkoxyalkyl-2,5-dimethyl-4-piperidols, which were then converted into the corresponding esters (acetates, propionates, benzoates).

2. 1-Carbethoxymethyl-2,5-dimethyl-4-piperidyl benzoate hydrochloride approaches novocaine in its anesthetic activity. The other compounds prepared show no significant physiological activity.

LITERATURE CITED

[1] I. N. Nazarov et al., J. Gen. Chem. 26, 2798, 2834 (1956).*

[2] Berger, Ziering and Lee, J. Org. Chem. 12, 894, 904 (1947); Ziering and Lee, J. Org. Chem. 12, 911 (1947).

[3] I. N. Nazarov and V. A. Rudenko, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1948, 610.

[4] I. N. Nazarov, D. V. Sokolov and V. N. Rakcheeva, Bull. Acad, Sci. USSR, Div. Chem. Sci. 1954, 80 (T. p. 65)**

[5] I. N. Nazarov, T. V. Sheremeteva and R. I. Kruglikova, J. Gen. Chem. 26, 3510 (1956).*

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Moscow Institute of Fine Chemical Technology

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*Original Russian pagination. See C. B. translation.

**T. p. = C. B. Translation pagination.

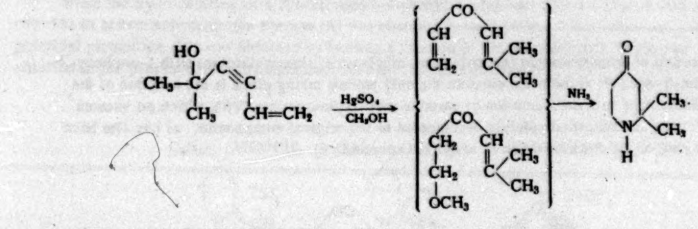
HETEROCYCLIC COMPOUNDS

50. SYNTHETIC PAIN-RELIEVING MATERIALS.

XIII. THE ACTION OF PRIMARY AMINES ON β, β-DIMETHYLDIVINYL KETONE AND 1-METHOXY-5-METHYL-4-HEXENE-3-ONE. THE ESTERS OF 1,2,2-TRIMETHYL-4-PHENYL-4-PIPERIDOL

I. N. Nazarov and S. M. Makin

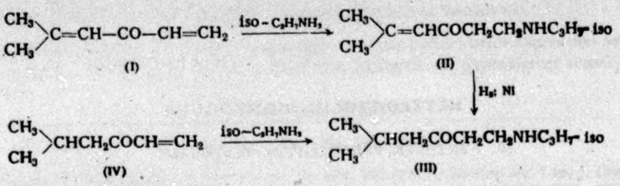
It has been shown in our laboratory that β, β-dimethyldivinyl ketone and 1-methoxy-5-methyl-4-hexene-3-one, which are readily obtained by the isomerization of dimethylvinylethinylcarbinol [1], react with aqueous ammonia to give 2,2-dimethyl-4-piperidone [2]:



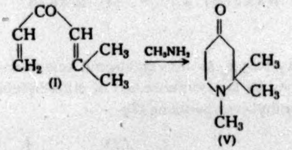
Since the reaction is accompanied by the formation of large quantities of tarry condensation products, the 2,2-dimethyl-4-piperidone could only be isolated in very small amount in the form of salts (picrate and oxalate).

Interest was also attached to the study of the action of primary aliphatic amines on β, β-dimethyldivinyl ketone and 1-methoxy-5-methyl-4-hexene-3-one with the aim of preparing 1-alkyl-2,2-dimethyl-4-piperidone which could then be used as starting products for the synthesis of physiologically active (pain-relieving) compounds. It turned out that this reaction depends to a considerable extent on the primary amine taken for the reaction and also on the temperature, and may lead either to the formation of the products of addition of the amines to the double bond (in mild conditions) or to the formation of 1-alkyl-2,2-dimethyl-4-piperidones.

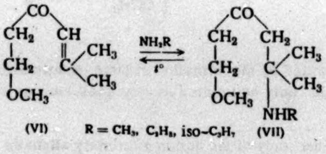
In the reaction of isopropylamine with β, β-dimethyldivinyl ketone (I) at room temperature the only process which takes place is the addition of the isopropylamine to the unsubstituted vinyl group, and in this way 1-isopropylamino-5-methyl-4-hexene-3-one (II) is formed (in 76 % yield). As has been shown earlier [3,4], the reaction of β, β-dimethyldivinyl ketone with aniline and secondary amines takes place in similar fashion. The unsaturated ketoamine (II) is also obtained by the reaction of isopropylamine with β,β-dimethyldivinyl ketone at a temperature of 60-65° for 6 hours. The yield in these conditions, however, is considerably lowered (31 %) and the reaction is accompanied by a great deal of tar formation. The structure of the unsaturated ketoamine (II) has been proved by converting it by hydrogenation to the saturated ketoamine (III), which has also been prepared by the addition of isopropylamine to vinyl isobutyl ketone (IV) [5,6]:



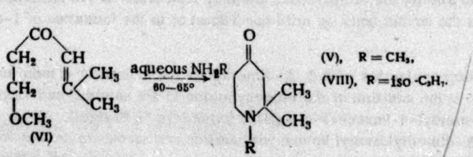
Methylamine reacts vigorously with β, β-dimethyldivinyl ketone (I) even at room temperature, but the corresponding unsaturated ketoamine cannot be detected in this case; a small quantity of 1,2,2,-trimethyl-4-piperidone (V) is obtained, while the greater part of the product is converted to a tar.



In the reaction of primary amines (methylamine, ethylamine, isopropylamine) with 1-methoxy-5-methyl-4-hexene-3-one (VI) at room temperature the only process taking place is the addition of the amine to the double bond with the formation of unstable methoxyketoamines (VII), which on vacuum distillation (6-7 mm) are almost completely decomposed to the original components, as has also been observed in the case of the diacetonamine of analogous structure [8].



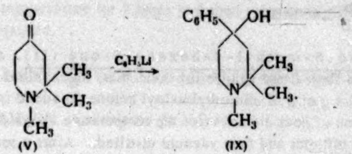
The reaction of 1-methoxy-5-methyl-4-hexene-3-one (VI) with aqueous solutions of primary amines (methylamine, isopropylamine) at 60-65° for 4-6 hours leads to the formation of 1-alkyl-2,2-dimethyl-4-piperidones (V) and (VIII) in yields of 20-30 %:



Methylamine reacts more readily in this reaction than isopropylamine, but a considerable amount of tar formation always takes place. Attempts to avoid tar formation by lowering the reaction temperature or reducing the time of heating did not give positive results, since when this was done the products were mixtures, difficult to separate, of the piperidones and the isomeric products of the addition to the unsubstituted vinyl group of the β, β-dimethyldivinyl ketone.

Thus the cyclization leading to γ-piperidones by the action of primary amines on β,β-dimethyldivinyl ketone proceeds less smoothly and with much lower yields than in the case of other divinyl ketones with substituents in both vinyl groups.

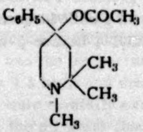
The action of phenyllithium on 1,2,2-trimethyl-4-piperidone (V) leads to the formation (in approximately 60% yield) of 1,2,2,-trimethyl 4-phenyl-4-piperidol (IX), whose esters were prepared for pharmacological tests.



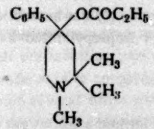
(V) (IX)

There is only one asymmetric carbon atom in the molecule of 1,2,2-trimethyl-4-phenyl-4-piperidol, so that it has only one racemic form, which melts at 116-117°.

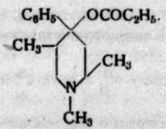
When the hydrochloride of 1,2,2-trimethyl-4-phenyl-4-piperidol (IX) was heated with acetyl chloride in acetic anhydride, the acetate (X) was obtained in good yield. 1,2,2-Trimethyl-4-phenyl-4-piperidyl propionate (XI) was obtained by heating a solution of the piperidol (IX) in benzene with propionyl chloride in the presence of fine magnesium turnings (Spasov's method [8]).



(X)



(XI)



(XII)

This last reaction is accompanied by the formation of a product of the dehydration of 1,2,2-trimethyl-4-phenyl-4-piperidol, whose structure was not determined.

The 1,2,2-trimethyl-4-phenyl-4-piperidyl propionate (XI) described above is the structural isomer of promedol (XII) [9] (1,2,5-trimethyl-4-phenyl-4-piperidyl propionate) and it was therefore interesting to compare their pain-relieving activity.

Pharmacological tests carried out in Prof. M. D. Mashkovsky's laboratory (S. Ordzhonikidze All-Union Chemical and Pharmaceutical Scientific Research Institute) showed that the hydrochloride of 1,2,2-trimethyl-4-phenyl-4-piperidyl propionate (XI) exhibits a powerful analgesic action, which is as great as that of morphine. Its pain-relieving action, however, is only 50-60% of that of promedol (XII). Thus when the methyl group is shifted from the 5 position to the 2 position of the piperidone nucleus in the promedol molecule, the pain-relieving activity is lowered by a factor of almost two.

The hydrochloride of the acetate (X), in doses of 5 and 10 mg/kg in tests on white rats, showed no change in the threshold of pain sensitivity, i. e. this compound shows practically no pain-relieving activity.

EXPERIMENTAL

1-Methoxy-5-methyl-4-hexene-3-one (VI). 1500 ml methyl alcohol, 40 g finely divided mercuric sulfate and 2000 g dimethyldivinyl ketone were placed in a three-necked five-liter flask fitted with reflux condenser, mechanical stirrer and thermometer. The mixture was stirred at 38-40° for 13 hours and during this time a further 35 g of mercuric sulfate was added in two portions (after 6 and 10 hours). A total of 75 g mercuric sulfate was thus added. The mixture was cooled, washed with saturated potassium carbonate solution and dried with sodium sulfate. When the product was vacuum distilled 2308 g (90%) of the previously described [11] 1-methoxy-5-methyl-4-hexene-3-one (VI) was obtained.

B. p. 76–79° (9 mm), n_D^{20} 1.4555.

The removal of methanol from the methoxyketone (VI) using p-toluenesulfonic acid led to the formation of β, β-dimethyldivinyl ketone (I).

B. p. 54° (15 mm), n_D^{20} 1.4800 [10].

1-Isopropylamino-5-methyl-4-hexene-3-one (II). a) 10 g isopropylamine was placed in a round-bottomed flask fitted with reflux condenser, mechanical stirrer and thermometer, 3 drops of water were added and 19.4 g of β, β-dimethyldivinyl ketone (I) added in small portions with stirring at such a rate that the evolution of heat did not raise the temperature above 60°. The reaction mass was left at room temperature for 20 minutes and then vacuum distilled. After a second distillation 21.7 g (76%) of 1-isopropylamino-5-methyl-4-hexene-3-one (II) was isolated in the form of a colorless liquid.

B. p. 68–69° (2.5 mm), n_D^{20} 1.4659, d_{20}^{20} 0.9015, MR 51.92; calc. 51.52.

Found %: N 8.49, 8.44. $C_{10}H_{19}ON$. Calculated %: N 8.29.

The hydrochloride of the ketoamine (II) was prepared by the action of dry hydrogen chloride on a solution of the base in absolute ether. After two recrystallizations from acetone it melted at 128-129°.

Found %: N 6.62, 6.68. $C_{10}H_{20}ONCl$. Calculated %: N 6.81.

b) When 22 g β, β-dimethyldivinyl ketone (I) was heated with 18 g of 66% aqueous isopropylamine solution at 60-65° for 6 hours, 10.6 g (31%) of 1-isopropylamino-5-methyl-4-hexene-3-one was obtained.

B. p. 64-65° (2 mm), n_D^{20} 1.4660, d_{20}^{20} 0.9015.

A considerable amount of the substance formed a tar.

1-Isopropylamino-5-methylhexane-3-one (III). a) 4.5 g of the unsaturated ketoamine (II) (b.p. 68-69° at 2.5 mm, n_D^{20} 1.4659) in 15 ml ethyl alcohol was hydrogenated in the presence of nickel catalyst. 650 ml of hydrogen (730 mm, 22°) was absorbed in 35 minutes. The catalyst was separated, the alcohol removed and the product vacuum distilled. 3 g of the saturated ketoamine (III) was obtained in the form of a colorless liquid.

B. p. 52° (2 mm), n_D^{20} 1.4365, d_{20}^{20} 0.8666, MR 51.72; calc. 51.99.

Found %: N 7.98, 7.82. $C_{10}H_{21}ON$. Calculated %: N 8.18.

The **hydrochloride** of this ketoamine had m. p. 85-86° (from acetone).

Found %: N 6.65, 6.71. $C_{10}H_{22}ONCl$. Calculated %: N 6.74.

b) 16 g vinyl isobutyl ketone (b. p. 61° at 44 mm, n_D^{20} 1.4270 [11]) was taken and 9 g isopropylamine was added dropwise over a period of 20 minutes with stirring (so that the temperature of the reaction mass did not exceed 50°), after which the reaction mixture was heated for 1 hour at 50-55° and then vacuum distilled. 12 g of 1-isopropylamino-5-methyl-hexane-3-one (III) was obtained.

B. p. 63° (3 mm), n_D^{20} 1.4350, d_{20}^{20} 0.8669.

The hydrochloride of the ketoamine obtained had m. p. 86-87° and gave no melting point depression with the previous specimen.

The action of methylamine on β, β-dimethyldivinyl ketone. 5 g of gaseous methylamine was passed slowly at 20° with steady stirring into 22 g β, β-dimethyldivinyl ketone. The mixture was left to stand at room temperature for 2 hours and then vacuum distilled. 5.0 g of 1,2,2-trimethyl-4-piperidone (V) was obtained.

B. p. 52-53° (2.5 mm), n_D^{20} 1.4688, d_{20}^{20} 0.9582 [12], MR 40.46; calc. 40.90.

Found %: N 10.05, 10.29. $C_8H_{15}ON$. Calculated %: N 9.94.

The picrate of the piperidone (V) was precipitated slowly on mixing alcoholic solutions of picric acid and the piperidone base. It was obtained after two recrystallizations from alcohol in the form of a yellow powder with m. p. 150° (decomp.).

Found %: N 15.15, 14.79. $C_{14}H_{18}O_8N_4$. Calculated %: N 15.12.

This experiment also gave 16.8 g of a condensation product with b. p. 70-140° (2.5 mm) which was not further studied.

The action of methylamine on 1-methoxy-5-methyl-4-hexene-3-one. a) 21.3 of freshly distilled 1-methoxy-5-methyl-4-hexene-3-one (VI) (b.p. 76-79°, 9mm, n_D^{20} 1.455) was placed in a three-necked flask fitted with mechanical stirrer, reflux condenser and thermometer, after which 20 g of 25% aqueous methylamine solution was added dropwise over a period of 15 minutes. Evolution of heat was observed and the temperature of the reaction mass rose to 35°. The reaction mass was left at room temperature for 1.5 hours and then made acid to congo red by treatment with 18% hydrochloric acid. The neutral products were carefully extracted several times with ether and the aqueous layer treated with potassium carbonate; the oil which rose to the surface was extracted with ether and dried with ignited sodium sulfate. The ether was removed by distillation under reduced pressure at the water pump at a bath temperature not exceeding 20° and the residue kept for 3 hours in vacuo at the oil pump (1.5 mm). 14.8 g of impure 1-methoxy-5-methyl-5-methylaminohexane-3-one (VII) was obtained in the form of a pale yellow liquid with an amine odor.

Found %: N 7.90, 7.95. $C_9H_{19}O_2N$. Calculated %: N 8.08.

The hydrochloride of this substance was an oil which did not crystallize.

When distilled in vacuo the product (VII) boiled at 68-70° (7 mm), n_D^{20} 1.4554 (weight 10.3 g) and had an odor of the original 1-methoxy-5-methyl-4-hexene-3-one (VI).

Found %: N 3.38, 3.54.

Similar results were obtained by the action of ethylamine and isopropylamine (at room temperature) on 1-methoxy-5-methyl-4-hexene-3-one (VI).

b) A mixture of 284 g of the methoxyketone (VI), 216 g of 30% aqueous methylamine solution and 250 ml methyl alcohol was heated in a steel ball for 4.5 hours at 60°. The reaction mass was then acidified with 18% hydrochloric acid to congo red and the methanol distilled off in vacuo. The neutral products were carefully extracted with ether and the aqueous solution treated with solid alkali. The oil which rose to the surface was extracted with ether and dried with sodium sulfate. When the product was vacuum distilled, 85 g of material with b. p. 70-80° (3.5 mm) was obtained. 105 g of tarry residue remained. After a second vacuum distillation, 64 g (22.5%) of pure 1,2,2-trimethyl-4-piperidone (V) was obtained.

B. p. 52-53° (2.5 mm), n^{20}_{D} 1.4688, d^{20}_{20} 0.9582.

The picrate of the 1,2,2-trimethyl-4-piperidone (V) obtained melted at 150° (decomp.) and gave no melting point depression with the picrate of piperidone (V) prepared by the action of methylamine on β, β-dimethyldivinyl ketone.

1- Isopropyl-2,2-dimethyl-4-piperidone (VIII). A mixture of 300g of the methoxyketone (VI), 250 ml methyl alcohol, 150 g isopropylamine and 300 ml water was heated in a steel ball at 63-68° for 6 hours and then treated as in the previous experiment. When the product was vacuum distilled, 72 g (20.5%) of 1-isopropyl-2,5-dimethyl-4-piperidone (VIII) with b. p. 58-60° (2 mm) was obtained and this crystallized in the receiver when distilled a second time. After two recrystallizations from benzene the 1-isopropyl-2,2-dimethyl-4-piperidone had m. p. 40-41°.

Found %: N 8.08, 8.04. $C_{10}H_{19}ON$. Calculated %: N 8.28.

The hydrochloride of the piperidone (VIII) was prepared by saturating an ethereal solution of the base with dry hydrogen chloride. After two recrystallizations from alcohol it had m. p. 138-139°.

Found %: Cl 17.17, 17.21. $C_{10}H_{20}ONCl$. Calculated %: Cl 17.32.

1,2,2,-Trimethyl-4-phenyl-4-piperidol (IX). 14.1 g 1,2,2-trimethyl-4-piperidone (V) was added over a period of one hour with cooling by a mixture of snow and salt to an ethereal solution of phenyllithium (prepared in the usual way from 2 g lithium and 20.6 g bromobenzene in 50 ml absolute ether). The reaction mass was then stirred for 6 hours at room temperature and for 2 hours with the ether boiling. The product was hydrolyzed with water (50 ml), extracted with ether, and the ether extracts treated with 10% hydrochloric acid to extract the base. The aqueous acid solution was treated with solid alkali, the oil which rose to the surface extracted repeatedly with ether and dried with ignited potassium carbonate. When the ether was distilled off the residue crystallized and from it was isolated 9.5 g of 1,2,2-trimethyl-4-phenyl-4-piperidol (IX) which after two recrystallizations from benzene melted at 116-117°. When the mother solution was distilled in vacuo 2.8 g of the original 1,2,2-trimethyl-4-piperidone with b. p. 56-60° (3 mm) and 3.5 g of 1,2,2-trimethyl-4-phenyl-4-piperidol with b. p. 125-130° (2.5 mm), which crystallized in the receiver and melted at 116-117°, were obtained. Total yield of 1,2,2-trimethyl-4-phenyl-4-piperidol (IX) 13 g (60%).

Found %: C 76.41, 76.47; H 9.60, 9.39; N 6.35; 6.24. $C_{14}H_{21}ON$. Calculated %: C 76.67; H 9.65; N 6.39.

The hydrochloride of 1,2,2-trimethyl-4-phenyl-4-piperidol (IX) was obtained by saturating an ethereal solution of the base with dry hydrogen chloride. After recrystallization from a mixture of alcohol and acetone it melted at 209-210°.

Found %: Cl 13.91, 13.97. $C_{14}H_{22}ONCl$. Calculated %: Cl 13.87.

1,2,2-Trimethyl-4-phenyl-4-piperidyl acetate (X). 2.7 g of 1,2,2-trimethyl-4-phenyl-4-piperidol hydrochloride (m. p. 209-210°), 6 ml acetyl chloride and 15 ml acetic anhydride were heated at 90-100° for 10 hours. The acetyl chloride and acetic anhydride were distilled off in vacuo and the residue which crystallized was washed with ether and dried in a vacuum desiccator. After two recrystallizations from acetone, 2.7 g of the hydrochloride of 1,2,2-trimethyl-4-phenyl-4-piperidyl acetate (X) was obtained in the form of long thin needles with m. p. 223-224°.

Found %: N 4.57, 4.47. $C_{16}H_{24}O_2NCl$. Calculated %: N 4.71.

1,2,2-Trimethyl-4-phenyl-4-piperidyl propionate (XI). a) A mixture of 10 g 1,2,2-trimethyl-4-phenyl-4-piperidol (m. p. 116-117°), 15 ml dry benzene, 35 ml propionyl chloride and 0.4 g magnesium turnings was heated with vigorous stirring for 5 hours at 60-65° until the precipitate initially formed had completely dissolved. The mixture was cooled, the propionyl chloride and benzene distilled off in vacuo, the residue washed with ether and dissolved in 20 ml water. The aqueous solution was treated with potassium carbonate, the oil which rose to the surface was extracted with ether and the ether extract dried with ignited potassium carbonate. Two distillations in vacuo yielded 4.4 g of the product of the dehydration of 1,2,2-trimethyl-4-phenyl-4-piperidol with b. p. 95-100° (3.5 mm), n_D^{20} 1.5547 (see experiment 6) and 5.3 g of 1,2,2-trimethyl-4-phenyl-4-piperidyl propionate (XI) with b.p. 138-142° (2.5 mm).

Found %: N 5.25, 5.29. $C_{17}H_{25}O_2N$. Calculated % N 5.09.

The hydrochloride of 1,2,2-trimethyl-4-phenyl-4-piperidyl propionate was obtained in the usual way and after three recrystallizations from acetone melted at 169.5-170°.

Found %: C 65.17, 65.29; H 8.51, 8.35; Cl 10.97, 11.15. $C_{17}H_{26}O_2NCl$. Calculated %: C 65.47; H 8.40; Cl 11.37.

b) A mixture of 4.9 g 1,2,2-trimethyl-4-phenyl-4-piperidol (m. p. 116-117°), 15 ml propionyl chloride, 15 ml dry benzene and 0.3 g magnesium turnings were heated with vigorous stirring at 95° for 10 hours. The reaction mass was then treated as in experiment a). 3.8 g of the product of dehydration of 1,2,2-trimethyl-4-phenyl-4-piperidol was obtained in the form of a colorless mobile liquid with b. p. 88-89° (3 mm), n_D^{20} 1.5545.

Found %: N 7.14, 7.13. $C_{14}H_{19}N$. Calculated % N 6.96.

The picrate melted at 130-132° (from alcohol).

Found %: N 12.74, 12.99. $C_{20}H_{22}O_7N_4$. Calculated %: N 13.01.

SUMMARY

A study has been made of the reaction of β, β-dimethyldivinyl ketone and 1-methoxy-5-methyl-4-hexene-3-one with primary amines and it has been shown that, depending on the temperature, the reaction leads to the formation of either 1-alkyl-2,2-dimethyl-4-piperidones or the products of the addition of the primary amine to the double bond (in mild conditions).

1,2,2-Trimethyl-4-phenyl-4-piperidol was prepared in 60% yield by the action of phenyllithium on 1,2,2-trimethyl-4-piperidone, and has been converted into its acetic and propionic esters. The latter was tested pharmacologically and found to show a high pain-relieving activity, as great as that of morphine but only half that of promedol.

LITERATURE CITED

[1] I. N. Nazarov et al., Bull. Acad. Sci. USSR, Div. Chem. Sci. 1940, 223, 453, 545; 1941, 314.

[2] I. N. Nazarov and A. Kh. Khomenko, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1944, 137.

[3] I. N. Nazarov and A. Kh. Khomenko, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1944, 226.

[4] I. N. Nazarov and A. Kh. Khomenko, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1945, 504.

[5] I. N. Nazarov and V. M. Romanov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1940, 453.

[6] E. Blaise and M. Maire, Compt. rend. 142, 216 (1906); I. N. Nazarov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1940, 552.

[7] Dictionary of Organic Compounds, 1949, I. 626.

[8] Spasov, Ber. 75, 779 (1942).

[9] I. N. Nazarov et al., Bull. Acad. Sci. USSR, Div. Chem. Sci. 5, 504 (1949); J. Gen. Chem. 26, 2798 (1956).*

[10] I. N. Nazarov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1940, 545.

[11] I. N. Nazarov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1940, 552.

[12] I. N. Nazarov, S. G. Matsoyan and S A. Vartanyan, J. Gen. Chem. 23, 1990 (1953).*

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M. V. Lomonosov Institute of Fine Chemical
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* Original Russian pagination. See C. B. translation.

HETEROCYCLIC COMPOUNDS

51. SYNTHETIC PAIN-KILLING SUBSTANCES

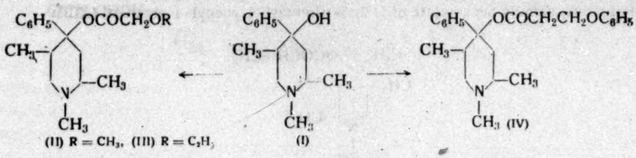
XIV. ESTERS OF 1,2,5-TRIMETHYL-4-PHENYL-4-PIPERIDOL WITH FUNCTIONAL GROUPS ON THE ACYL RADICAL. ANALOGS OF PROMEDOL AND ISOPROMEDOL. I.

I. N. Nazarov, S. M. Makin and A. F. Grapov

In previous papers from our laboratory we communicated on the synthesis of the stereoisomeric 1,2,5-trimethyl-4-phenyl-4-piperidols, which were converted into various esters by esterification, mainly with the simple aliphatic acids (acetic, propionic, etc.) [1, 2]. It was shown that some of these esters, especially the propionates, show high pain-killing efficacy, exceeding by many times the action of the natural alkaloid, morphine. It seemed of interest to also obtain the esters of 1,2,5-trimethyl-4-phenyl-4-piperidol with various functional groups on the acyl radical (the alkoxyl, alkyl sulfide and amine groups, and also the halides and double bonds), and to establish the influence of these groups on the physiological activity of the obtained compounds. The acyl radical is an extremely "sensitive" spot in the molecule of the 4-phenyl-4-piperidol esters. Slight changes in its structure lead to sharp changes in the physiological activity. It is known that the propionates of the 4-phenyl-4-piperidols show the maximum analgesic activity. A shortening of the propionyl radical to the methylene group, i.e., the esterification of 4-phenyl-4-piperidols with acetic acid, leads to a sharp reduction in the pain-killing activity [2, 3]. A lengthening of the propionyl radical, i.e., the esterification of 4-phenyl-4-piperidols with such acids as butyric, valeric and caproic acids, also leads to a sharp reduction in the pain-killing activity in measure with lengthening of the acyl radical [2, 3].

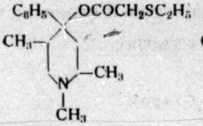
On the example of the methoxy-and ethoxyacetates of 1,2,5-trimethyl-4-phenyl-4-piperidol synthesized by us, we wanted to establish the influence of alkoxyl groups in the acetyl radical on the physiological (pain-killing) activity of the indicated esters. In addition, the introduction of methoxy and ethoxy groups lengthens the acetyl radical, i.e., up to a certain degree it imitates in its magnitude the acyl radical of the propionates and butyrates, which show a much greater pain-killing activity than do the corresponding acetates. Consequently, a testing of the pain-killing activity of these compounds will answer the question of whether only the total length of the acyl chain is important, or whether it must necessarily be a hydrocarbon chain.

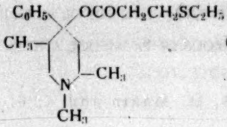
The esterification of 1,2,5-trimethyl-4-phenyl-4-piperidol (I) with the chlorides of the corresponding acids by the Spasov method [4] gave (in 60-75% yields) the methoxyacetate (II) and ethoxyacetate (III). In both of these cases, as well as for all of the subsequent cases, the high-melting γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol (m. p. 107-108°), being the most readily available [1], was taken for esterification.

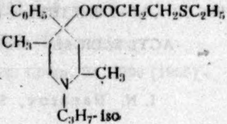

(II) R = CH_3, (III) R = C_2H_5 (I) (IV)

In a similar manner the esterification of 1,2,5-trimethyl-4-phenyl-4-piperidol (I) with β-phenoxypropionyl chloride gave the β-phenoxypropionic ester (IV).

It was also of interest to obtain the 4-phenyl-4-piperidol esters containing sulfur in the acyl radical. In this connection it should be mentioned that the sulfur (sulfonic) analogs of lidol show comparatively high pain-killing activity (equal to lidol) and very low toxicity [5]. The action of the corresponding acid chlorides on benzene solutions of 1,2,5-trimethyl-4-phenyl-4-piperidol (I) in the presence of metallic magnesium gave the ethylmercaptoacetate (V) and the β-ethylmercaptopropionate (VI). The β-ethylmercaptopropionate (VII) was also obtained in a similar manner by the esterification of 1-isopropryl-2, 5-dimethyl-4-phenyl-4-piperidol.

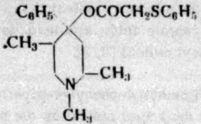

(V)

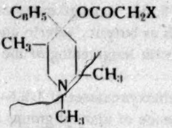

(VI)

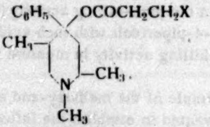

(VII)

The phenylthioglycolic ester (VIII) was obtained by long heating of the piperidol (I) hydrochloride with phenylthioglycoloyl chloride in chloroform solution. The reaction of phenylthioglycoloyl chloride with the free piperidol (I) base leads to very pronounced tarring of the reaction mass.

The heating of a chloroform solution of the piperidol (I) hydrochloride with the corresponding acid chlorides also gave the chloroacetate (IX), bromoacetate (X), β-chloropropionate (XI) and β-bromopropionate (XII):

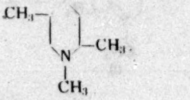

(VIII)


X = Cl (IX),
X = Br (X).


X = Cl (XI),
X = Br (XII).

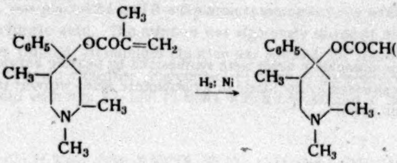
It should be mentioned that the β-chloro- and β-bromo-propionates are obtained much more easily and in better yields than are the chloro- and bromoacetates (the total yield of which is only 10-15%). Completely negative results are obtained when other methods (for example, the Spasov method of esterification in pyridine medium) are used to prepare these esters.

The reaction of β-chloropropionyl chloride with 1,2,5-trimethyl-4-phenyl-4-piperidol (I) under the conditions of the Spasov reaction gave, instead of the desired β-chloropropionate (XI), the product of its dehydrochlorination, namely the acrylate of 1, 2, 5-trimethyl-4-phenyl-4-piperidol (XIII):


(XIII)

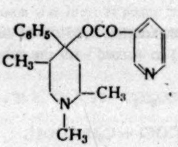
The acrylate (XIII) is probably obtained during the distillation of the β-chloropropionate (XI) obtained in the reaction (bath temperature 160-165°, vacuum 0.2mm). The structure of the acrylate (XIII) was proved by its hydrogenation to the known propionate (promedol). Numerous attempts to synthesize the acrylate (XIII) by the direct reaction of acryloyl chloride with 1,2,5-trimethyl-4-phenyl-4-piperidol (I) proved unsuccessful, since a tarry product, incapable of being vacuum-distilled, was obtained in all cases.

However, the methacrylate (XIV) is obtained in very good yield by the direct reaction of methacryloyl chloride with 1,2,5-trimethyl-4-phenyl-4-piperidol (I), both under the conditions of the Spasov reaction and by the simple mixing of methacryloyl chloride with a chloroform solution of the piperidol (I). Catalytic hydrogenation of the methacrylate (XIV) gives the isobutyrate (XV), which was synthesized earlier in our laboratory by the reaction of isobutyryl chloride with 1,2,5-trimethyl-4-phenyl-4-piperidol (I):

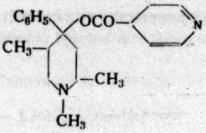


(XIV) (XV)

The reaction of 1,2,5-trimethyl-4-phenyl-4-piperidol (I) with the chlorides of nicotinic and isonicotinic acids in chloroform solution, even at room temperature, easily yields the nicotinic (XVI) and isonicotinic (XVII) esters:



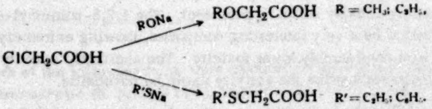
(XVI)



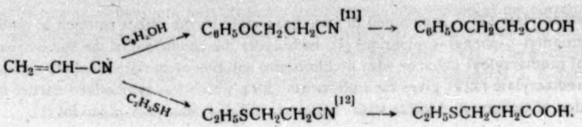
(XVII)

These esters are of interest for reasons other than their manifested pain-killing and anesthetic properties. As is known, some nicotinic acid derivatives show vitaminic activity (vitamin PP), and also the ability to exert a stimulant action on the central nervous system and to lower the blood pressure. Among the isonicotinic acid derivatives are found interesting antituberculous compounds [6]. A series of different acids and their chlorides were needed for the synthesis of the above described esters.

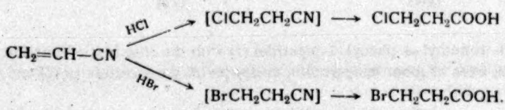
All of the acetic acid derivatives were synthesized from chloroacetic acid by the following scheme:



The methoxyacetic [7], ethoxyacetic [8], ethylthioglycolic [9] and phenylthioglycolic [10] acids were obtained in this manner. The β-phenoxy- and β-ethylmercaptopropionic acids were obtained from acrylonitrile in the following manner: .



The β-chloro-and β-bromopropionic acids were synthesized by heating acrylonitrile with a 3-fold (on a molar basis) amount of concentrated hydrochloric or hydrobromic acid, without isolation of the β-halopropionitriles from the reaction mass:



The chlorides of methoxyacetic, ethoxyacetic, bromoacetic, acrylic and methacrylic acids were obtained by heating these acids with benzoyl chloride [13] in accord with the scheme:

$$RCOOH + C_6H_5COCl \longrightarrow RCOCl + C_6H_5COOH.$$

The chlorides of β-phenoxypropionic, β-ethylmercaptopropionic, ethylthioglycolic, β-chloropropionic, β-bromopropionic, phenylthioglycolic, nicotinic [14] and isonicotinic [14] acids were obtained by reacting the respective acids with thionyl chloride.

Pharmacological Test Results

The 1,2,5-trimethyl-4-phenyl-4-piperidol esters containing halogen, alkoxy and alkyl sulfide groups in the acyl radical were practically devoid of morphinelike activity. The acrylate (XIII) and methacrylate (XIV) showed high pain-killing activity, close to the activity of morphine. However, both of these esters are less active than promedol (1,2,5-trimethyl-4-phenyl-4-piperidol propionate): the acrylate shows ½, and the methacrylate 1/3 the pain-killing activity shown by promedol. The 1,2,5-trimethyl-4-phenyl-4-piperidol β-phenoxypropionate (IV) proved to be a very interesting compound, showing extremely high anesthetic activity, equal to that of dicaine, with considerably lower toxicity. The anesthetic activity shown by 1% of the β-chloropropionate (XI) is approximately twice the activity shown by novocaine.

All of the compounds were tested as the hydrochlorides. The pharmacological testing was done in the Pharmacological Laboratory of the S. Ordzhonikidze All-Union Scientific-Research Chemical-Pharmaceutical Institute under the supervision of Prof. M. D. Mashkovsky.

EXPERIMENTAL

β-Chloropropionic Acid. Into a three-necked flask, fitted with mechanical stirrer and reflux condenser, was charged 53 g of acrylonitrile and 300 ml of concentrated hydrochloric acid The reaction mixture was stirred at 90-100° for 4 hours. After cooling, the formed ammonium chloride was filtered, and the filtrate was evaporated in vacuo. The second crop of ammonium chloride was filtered, the product extracted with ether, dried over anhydrous sodium sulfate, and vacuum-distilled. We obtained 55 g of β-chloropropionic acid with b.p. 92-93° (9 mm), which crystallized in the receiver.

The β-bromopropionic acid was obtained in a similar manner.

β-Ethylmercaptopropionic Acid. In a three-necked flask, fitted with mechanical stirrer, reflux condenser and thermometer, was placed 84 g of β-ethylmercaptopropionitrile with b.p. 108-110° (19 mm) and 140 g of concentrated hydrochloric acid. The mixture was vigorously stirred at 80° for 3.5 hours, and then for 40 minutes at 100°. The formed ammonium chloride was filtered, the solution extracted with ether, and the ether extract dried over calcium chloride. Vacuum-distillation of the product gave 82 g (84 %) of β-ethylmercaptopropionic acid with b.p. 97-100° (2 mm), which crystallized in the receiver as long needles with m. p. 28-30°.

Found %: C 44.62, 44.65; H 7.51, 7.24; S 23.25, 23.27. $C_5H_{10}O_2S$. Calculated %: C 44.75; H 7.51; S 23.89.

β-Phenoxypropionic acid was obtained from β-phenoxyproprionitrile in a similar manner (in 95% yield).

β-Ethylmercaptopropionyl Chloride. In a round-bottomed flask, fitted with reflux condenser and calcium chloride tube, was placed 53.4 g of β-ethylmercaptopropionic acid with b. p. 100-103° (2.5 mm) and 47.6 g of thionyl chloride. The mixture was kept at room temperature for 5 hours, and then it was heated at 40° for 1.5 hours. Vacuum-distillation of the product gave 58.6 g (96%) of β-ethylmercaptopropionyl chloride with b. p. 80-81° (11 mm).

Found %: C 39.30, 39.47; H 5.77, 5.92. C_5H_9OSCl. Calculated %: C 39.35; H 5.94.

Using a 1 $^1/_2$-2-fold amount of thionyl chloride, the chlorides of the following acids were obtained in a similar manner in high yields: β-chloropropionic acid with b. p. 72-75° (63 mm), β-bromopropionic acid with b. p. 110-112° (190 mm), β-phenoxypropionic acid with b. p. 98° (2 mm), and phenylthioglycolic acid with b. p. 120-123° (12 mm).

Methoxyacetyl Chloride. A mixture of 29 g of methoxyacetic acid with b. p. 103-104° (17 mm) and 64 ml of benzoyl chloride was heated in a Favorsky flask. The fraction boiling up to 132° was slowly distilled from the mixture, and then redistilled (in the presence of 1.5 ml of dimethylaniline). The yield of methoxyacetyl chloride with b. p. 109-112° (748 mm). was 24.7 g (70.5%).

Found %: C 32.56, 32.76; H 4.71, 5.26. $C_3H_5O_2Cl$. Calculated %: C 33.21; H 4.61.

The chlorides of the following acids were obtained in good yields by this method: ethoxyacetic (b. p. 125-129°), bromoacetic (b. p. 115-117°), acrylic (b.p. 74-77 °) and methacrylic acids (b.p. 98-100°)

1,2,5-Trimethyl-4-phenyl-4-piperidol Methoxyacetate (II). A mixture of 6 g of 1,2,5-trimethyl-4-phenyl-4-piperidol (b. p. 107-108°), 7 ml of methoxyacetyl chloride (b. p. 109-112°), 7.5 ml of dry benzene and 0.3 g of magnesium turnings was stirred for 3.5 hours at 80-90°. After cooling, the resulting crystalline precipitate was filtered, washed with ether, dissolved in 30 ml of water, and treated with potash. The floating oil was repeatedly extracted with ether and dried over fused sodium sulfate. Vacuum-distillation of the product gave 6 g (75.3%) of 1,2,5-trimethyl-4-phenyl-4-piperidol methoxyacetate (II) as a colorless liquid with b. p. 138-140°(1 mm).

Found %: N 5.04, 5.01. $C_{17}H_{25}O_3N$. Calculated %: N 4.80.

The hydrochloride of this ester was obtained by saturating an ether solution of the free base with dry hydrogen chloride. M. p. 211-212° (from alcohol-acetone mixture).

Found %: N 4.18, 4.27; Cl 10.98, 11.00. $C_{17}H_{26}O_3NCl$. Calculated %: N. 4.27; Cl 10.82.

1,2,5-Trimethyl-4-phenyl-4-piperidol Ethoxyacetate (III). A mixture of 8 g of 1,2,5-trimethyl-4-phenyl-4-piperidol, 13 ml of ethoxyacetyl chloride (b. p. 125-129°), 10 ml of dry benzene and 0.3 g of magnesium was heated for 10.5 hours at 95-100°. Then the reaction mass was worked up the same as in the previous experiment. Distillation of the product gave 1.3 g of starting piperidol with b. p. 113-120° (0.2 mm), which crystallized in the receiver, and 6.1 g of 1,2,5-trimethyl-4-phenyl-4-piperidol ethoxyacetate (III) as a noncrystallizing oil with b. p. 120-122° (0.2 mm).

The hydrochloride of the ethoxyacetate (III) was obtained in the usual manner. After two recrystallizations from a mixture of acetone and alcohol it melted at 192-193°.

Found %: N. 4.22, 4.34. $C_{18}H_{28}O_3NCl$. Calculated %: N 4.10.

1,2,5-Trimethyl-4-phenyl-4-piperidol β-Phenoxypropionate (IV). A mixture of 11 g of 1,2,5-trimethyl-4-phenyl-4-piperidol, 15 ml of dry benzene, 25 g of β-phenoxypropionyl chloride with b. p. 96-98° (2 mm) and 0.3 g of magnesium turnings was stirred at 100-102° for 10 hours. Then the reaction mass was treated with 35 ml of water, and the mixture worked up the same as in the previous experiments. Vacuum-distillation of the reaction product gave the following fractions: 1st, 90-120° (2 mm), 1.8 g; 2nd, 120-128° (1 mm), 3.5 g; 3rd, 182-185° (0.5 mm), 7.3 g; undistilled residue 1.2 g. The third fraction is 1,2,5-trimethyl-4-phenyl-4-piperidol β-phenoxypropionate (IV).

Found %: N 4.28, 4.29. $C_{23}H_{29}O_3N$. Calculated %: N 3.81.

The hydrochloride of the β-phenoxypropionate (IV) was obtained in the usual manner and melted at 181-182.5° (from acetone).

Found %: N 3.53, 3.52. $C_{23}H_{30}O_3NCl$. Calculated %: N 3.46.

The mixture of the β-phenoxypropionate (IV) hydrochloride with the hydrochloride of the starting alcohol (m. p. 157-159°) melted at 126-131°.

1,2,5-Trimethyl-4-phenyl-4-piperidol Ethylmercaptoacetate (V). A mixture of 10 g of 1,2,5-trimethyl-4-phenyl-4-piperidol, 15.9 g of ethylmercaptoacetyl chloride with b. p. 53-55° (8 mm), 0.3 g of magnesium turnings and 11 ml of dry benzene was heated for 9 hours at 85-98°. After cooling, the benzene was vacuum-distilled, and the residue was dissolved in water and treated with soda to isolate the free base. We obtained 1.9 g of starting piperidol with b. p. 113-120° (1 mm) and 3.05 g of 1,2,5-trimethyl-4-phenyl-4-piperidol ethylmercaptoacetate (V) as a yellowish oil with b. p. 149-151° (1 mm).

Found %: N 4.29, 4.52. $C_{18}H_{27}O_2NS$. Calculated %: N 4.35.

The hydrochloride of the ethylmercaptoacetate (V) after recrystallization from acetone was obtained as white needles with m.p. 178-179°.

Found %: C 59.90, 60.13; H 7.77, 7.84. $C_{18}H_{28}O_2NClS$. Caclculated %: C 60.40; H 7.70.

1,2,5-Trimethyl-4-phenyl-4-piperidol β-Ethylmercaptopropionate (VI). A mixture of 10.9 g of 1, 2,5-trimethyl-4-phenyl-4-piperidol, 15 ml of dry benzene, 0.3 g of magnesium turnings and 19 g of β-ethylmercaptopropionyl chloride with b. p. 80-81° (11 mm) was stirred at 80-90° for 7 hours, and then worked up the same as in the preceding experiments. Distillation of the product gave a fraction with b. p. 175-178° (2 mm), which was 1,2,5-trimethyl-4-phenyl-4-piperidol β-ethylmercaptopropionate (VI). Yield 4.8 g.

Found %: N 4.03, 4.15. $C_{19}H_{29}O_2NS$. Calculated %: N 4.17.

The hydrochloride was obtained as coarse colorless crystals, after two recrystallizations from dry acetone melting at 171-172°.

Found %: C 61.37, 61.40; H 8.02, 8.12; S 8.26, 8.30. $C_{19}H_{30}O_2NClS$. Calculated %: C 61.35; H 8.13; S 8.62.

1-Isopropyl-2,5-dimethyl-4-phenyl-4-piperidol β-Ethyl-mercaptopropionate (VII). In a three-necked flask, fitted with mechanical stirrer, reflux condenser and thermometer, was mixed 8.2 g of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidol, 10 ml of dry benzene, 12.7 g of β-ethylmercaptopropionyl chloride with b. p. 80-81° (11 mm) and 0.2 g of magnesium turnings. The reaction mass was heated at 93-95° for 6 hours and then worked up in the usual manner. Distillation of the substance gave a fraction with b. p. 179-181° (0.5 mm), being 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidol β-ethylmercaptopropionate (VII). Yield 3.8 g.

Found %: N 4.10, 4.21. $C_{21}H_{33}O_2NS$. Calculated %: N 3.85.

The hydrochloride was obtained as coarse crystals with m. p. 160-161.5° (from acetone).

Found %: N 3.34, 3.33. $C_{21}H_{34}O_2NClS$. Calculated %: N 3.50.

1,2,5-Trimethyl-4-phenyl-4-piperidol Phenylthioglycolate (VIII). A mixture of 6 g of 1,2,5-trimethyl-4-phenyl-4-piperidol hydrochloride, 5 g of phenylthioglycoloyl chloride with b. p. 121-123° (12 mm) and 4.5 ml of chloroform was heated at 120-140° for 14 hours. To the mixture after cooling was added 2 ml of ether; the resulting crystals were filtered, washed with ether, and after repeated recrystallization from acetone we obtained 0.5 g of 1,2,5-trimethyl-4-phenyl-4-piperidol phenylthioglycolate (VIII) hydrochloride as colorless crystals with m. p. 166-167°.

Found %: N 3.57, 3.38. $C_{22}H_{28}O_2NClS$. Calculated %: N 3.45.

All of the mother liquors were combined, evaporated, washed well with ether, dissolved in water, treated with potash, and extracted with ether. The ether extract was dried over anhydrous sodium sulfate and then vacuum-distilled. We obtained 1.7 g of 1,2,5-trimethyl-4-phenyl-4-piperidol phenylthioglycolate as a viscous oily liquid with b. p. 180-185° (1.5 mm).

Found %: N 3.26, 3.30. $C_{22}H_{27}O_2NS$. Calculated %: N 3.79.

1,2,5-Trimethyl-4-phenyl-4-piperidol Chloroacetat (IX). A mixture of 2 g of 1,2,5-trimethyl-4-phenyl-4-piperidol hydrochloride, 3ml of chloroacetyl chloride and 3 ml of chloroform was heated at 80° for 17 hours. After removal of the chloroform and excess chloroacetyl chloride by vacuum-distillation the mixture was treated with 2 ml of ether. The resulting crystals were filtered, washed with acetone, and recrystallized from alcohol. We obtained 0.4 g of the chloroacetate (IX) hydrochloride with m. p. 214-215°.

Found %: N 4.29, 4.35. $C_{16}H_{23}O_2NCl_2$. Calculated %: N 4.12.

1,2,5-Trimethyl-4-phenyl-4-piperidol Bromoacetate (X). A mixture of 6 g of 1,2,5-trimethyl-4-phenyl-4-piperidol hydrochloride, 4 g of bromoacetyl chloride (b. p. 131-133°) and 4 ml of chloroform was heated for 14 hours at 120-140°. After removal of the chloroform and excess bromoacetyl chloride by vacuum-distillation the residue was treated with 10 ml of acetone. The resulting crystals were filtered, washed with acetone and recrystallized from alcohol. The yield of the bromoacetate (X) hydrochloride with m. p. 201.5-202° was 0.3 g.

Found %: N 3.74, 3.79. $C_{16}H_{23}O_2NClBr$. Calculated %: N 3.72.

1,2,5-Trimethyl-4-phenyl-4-piperidol β-Bromopropionate (XII). A mixture of 8 g of 1,2,5-trimethyl-4-phenyl-4-piperidol hydrochloride, 7 g of β-bromopropionyl chloride with b. p. 106-110° (170 mm) and 5.5 ml of chloroform was heated for 17 hours at 100-120°. After cooling the resulting crystals were filtered, washed with ether, and vacuum-dried. We obtained 3.8 g of β-bromopropionate (XII) with m. p. 163-167°. Repeated recrystallization from alcohol gave 3.2 g of product with m. p. 169.5-170°.

Found %: N 3.87, 3.63; Cl 9.29, 8.94. $C_{17}H_{25}O_2NClBr$. Calculated %: N 3.57; Cl 9.07.

1,2,5-Trimethyl-4-phenyl-4-piperidol β-Chloropropionate (XI). A mixture of 8 g of 1,2,5-trimethyl-4-phenyl-4-piperidol hydrochloride, 5 ml of chloroform and 8 ml of β-chloropropionyl chloride with b. p. 63° (42 mm) was heated for 15 hours at 90°. Several drops of dry ether were added after cooling, and the obtained crystals were filtered. Two recrystallizations from an acetone-alcohol mixture gave 5.3 g of the β-chloropropionate (XI) hydrochloride with m. p. 178-179°.

Found %: N 4.26, 4.02; C 58.88, 58.46; H 7.27, 7.20. $C_{17}H_{25}O_2NCl_2$. Calculated %: N 4.04; C 58.96; H 7.28.

1,2,5-Trimethyl-4-phenyl-4-piperidol Acrylate (XIII). To a mixture of 8 g of 1,2,5-trimethyl-4-phenyl-4-piperidol, 10 ml of dry benzene and 0.3 g of magnesium turnings was added in 0.5 hour, in drops and with constant stirring, 17 g of β-chloropropionyl chloride with b. p. 58° (30 mm). Then the reaction mixture was stirred for 5 hours at 95°, 25 ml of water was added, the water solution was repeatedly washed with ether, treated with soda, the floating oil thoroughly extracted with ether and chloroform, dried over sodium sulfate, and vacuum-distilled. We obtained the fractions: 1st, b. p. 90-128° (1 mm), 1.1 g; 2nd, b. p. 128-130° (0.2 mm) 2.4 g, and 3 g of nondistillable residue.

The 2nd fraction was an oily liquid, failing to crystallize on standing, free of halogen, it was the acrylate (XIII).

Found %: N 5.15, 5.17. $C_{17}H_{23}O_2N$. Calculated %: N 5.12.

The hydrochloride of the acrylate (XIII) was obtained in the usual manner, and after two recrystallizations from acetone melted at 215-216°.

Found %: N 4.40, 4.17. $C_{17}H_{24}O_2NCl$. Calculated %: N 4.52.

Hydrogenation of the hydrochloride in alcohol using Pd catalyst gave the hydrochloride of 1,2,5-trimethyl-4-phenyl-4-piperidol propionate, melting at first at 199-200°, and then at 221-222° when melted a second time, and not showing a melting point depression with the authentic specimen [2].

1,2,5-Trimethyl-4-phenyl-4-piperidol Methacrylate (XIV.) a) A mixture of 10.9 g of 1,2,5-trimethyl-4-phenyl-4-piperidol, 10 ml of dry benzene, 13 g of methacryloyl chloride (b. p. 95-98°) and 0.3 g of fine magnesium turnings was stirred at the boil for 10 hours. The excess chloride and the benzene were vacuum-distilled, the residue was dissolved in 20 ml of water, thoroughly washed with ether, treated with soda, the floating oil extracted with ether, dried over anhydrous sodium sulfate, and vacuum-distilled. We obtained 10.5 g of 1,2,5-trimethyl-4-phenyl-4-piperidol methacrylate as a colorless viscous liquid with b. p. 120-122° (0.2 mm).

Found %: N 4.96, 5.00. $C_{18}H_{25}O_2N$. Calculated %: N 4.87.

The hydrochloride of the methacrylate (XIV), after several recrystallizations from acetone, melted at 231-232°.

Found %: N 4.12, 4.27; Cl 10.60, 11.18. $C_{18}H_{26}O_2NCl$. Calculated %: N 4.32; Cl 19.95.

b) To a solution of 1 g of 1,2,5-trimethyl-4-phenyl-4-piperidol in 1.5 ml of dry chloroform was added, in drops, 1.5 ml of methyacryloyl chloride. The mixture was let stand for a day. The product crystallized when several drops of ether were added. We obtained 0.85 g of the methacrylate (XIV) hydrochloride with m. p. 231-232°, not showing a melting point depression with the preceding specimen.

1,2,5-Trimethyl-4-phenyl-4-piperidol Isobutyrate (XV). A solution of 4.5 g of 1,2,5-trimethyl-4-phenyl-4-piperidol methacrylate (XIV) with b. p. 120-122° (0.2 mm) in 20 ml of anhydrous ethyl alcohol was hydrogenated in the presence of skeletal nickel catalyst. The theoretical amount of hydrogen was absorbed in 15 hours. The catalyst was filtered, the alcohol evaporated in vacuo, while the residue was dissolved in 100 ml of absolute ether and saturated with dry hydrogen chloride. The resulting isobutyrate (XV) hydrochloride precipitate, after three recrystallizations from acetone, melted at 207-208°, and did not give a m. p. depression with the earlier described specimen [2]. Yield 4 g.

Found %: N 4.34, 4.64. $C_{18}H_{28}O_2NCl$. Calculated %: N 4.30.

1,2,5-Trimethyl-4-phenyl-4-piperidol Nicotinate (XVI). To 7 g of 1,2,5-trimethyl-4-phenyl-4-piperidol in 7 ml of dry chloroform was added in small portions 5.2 g of nicotinoyl chloride with b. p. 87-88° (11 mm). Self-heating of the mixture to 50-55° was observed. The reaction mixture was let stand for a day. The crystalline nicotinate (XVI) monohydrochloride was filtered, washed with ether, and after two recrystallizations from acetone melted at 193-195°.

Found %: N 7.43, 7.44. $C_{20}H_{25}O_2N_2Cl$. Calculated %: N 7.76.

A solution of 2.2 g of the nicotinate (XVI) monohydrochloride in water was treated with ammonia, and the product was extracted with ether. After removal of the ether by evaporation the crystalline residue was recrystallized twice from isooctane to give 1.5 g of pure nicotinate (XVI) with m. p. 106-107.5°.

Found %: N 8.80, 8.40. $C_{20}H_{24}O_2N_2$. Calculated %: N 8.63.

The mixture of this substance with the starting piperidol (I) melted at 72-78°.

1,2,5-Trimethyl-4-phenyl-4-piperidol Isonicotinate (XVII). To a solution of 8 g of 1,2,5-trimethyl-4-phenyl-4-piperidol in 7 ml of chloroform was added 5.5 g of isonicotinoyl chloride, and the mixture was let stand for a day. The product was dissolved in water, washed with ether, treated with soda, the floating oil extracted with ether, and the ether extract dried over anhydrous potash. The product crystallized when the ether was distilled off. Several recrystallizations from benzine with the use of activated carbon gave 1.75 g of 1,2,5-trimethyl-4-phenyl-4-piperidol isonicotinate (XVII) with m. p. 134-135°.

Found %: N 8.58, 8.39. $C_{20}H_{24}O_2N_2$. Calculated %: N 8.64.

SUMMARY

A number of 1,2,5-trimethyl-4-phenyl-4-piperidol esters were synthesized, containing in the acyl radical (acetyl, propionyl) the alkoxyl, phenoxyl and alkyl sulfide groups, and also the halides, nitrogen and double bonds. It was shown that the introduction of the indicated groups in the acyl radical of the acetates and propionates of 1,2,5-trimethyl-4-phenyl-4-piperidol sharply reduces or completely destroys the analgesic activity of these compounds.

Of the described esters only the acrylate (XII) and methacrylate (XIV) show substantial pain-killing action, equal to 35-50% of the activity shown by promedol, while all of the other esters are practically devoid of morphinelike activity. Of all of the studied esters of the 4-phenyl-4-piperidols the greatest analgesic activity is shown by the propionates.

LITERATURE CITED

[1] L N. Nazarov, V. Ya. Raigorodskaya and V. A. Rudenko, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1949, 504.

[2] I. N. Nazarov, N. S. Prostakov, V. N. Rudenko and N. I. Shvetsov, J. Gen. Chem. 26, 2798*(1956).

[3] K. Jensen, F. Lindquist and C. Wolffbrand, Dansk. Tidsskr. Farm. 17, 173 (1943); Chem. Zentr. 1944, I, 297; A. Ziering, L. Berger, S. D. Heineman and J. Lee, J. Org. Chem. 12, 894 (1947); L. Berger, A. Ziering and J. Lee, J. Org. Chem. 12,904 (1947).*

[4] A. Spasov, Ber. 75, 779 (1942).

[5] J. Buchi, M. Prost, H. Eichenberger and R. Lieberherr, Helv. Chim. Acta 35, 1527 (1952); 36, 814 (1953).

[6] N. A. Preobrazhensky and E. I. Genkin, Chemistry of Organic Medicinals (State Chem. Press, 1953), p.132.

[7] W. Heintz, Ann. Physik 109, 305 (1834).

[8] Organic Syntheses Coll. Vol. II, p. 607 (Foreign Lit. Press, 1944).

[9] L. Ramberg, Ber. 40, 2588 (1907).

[10] L. Ramberg, Z. physik.Chem. 34, 562 (1900).

[11] A. H. Cook and K. J. Reed, J. Chem. Soc. 1945, 920; A. N. Kost and V. G. Yashunsky, J. Gen. Chem. 23, 230 (1953).*

[12] C. Hurd and L. Gershbein, J. Am. Chem. Soc. 69, 2328 (1947).

[13] a) H. C. Brown, J. Am. Chem. Soc. 60, 1325 (1938); b) G. H. Stempel, R. P. Cross and R. P. Mariella, J. Am. Chem. Soc. 72, 2299 (1950).

[14] a) H. Meyer and R. Graf, Ber. 61, 2205 (1928); b) E. Spath and H. Spitzen, Ber. 59, 1479 (1926).

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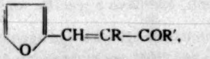
FURAN COMPOUNDS

VII. TWO-STAGE HYDROGENATION OF FURFURYLIDENE KETONES

Z. V. Til, I. Markushina, K. Sapunar and A. A. Ponomarev

The catalytic hydrogenation of furan compounds is the subject of numerous studies [1, 2]. A study of these reactions, proceeding, depending on the conditions, with the formation of a wide gamut of various hydrogenation products, is not only of preparative, but also of great theoretical interest [3, 4].

Many of the tetrahydrofuran and aliphatic substances, formed in the hydrogenation of even the simplest furan compounds, have found practical use as such and also as intermediates. Extremely intriguing as starting materials for such syntheses are the furfurylidene ketones of type



representing readily available derivatives of furfural.

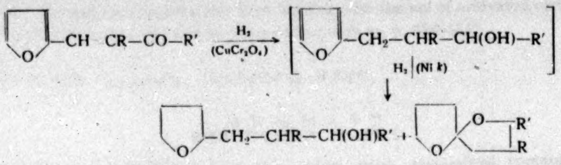
Most of the studies published in the literature on the hydrogenation of unsaturated furan ketones are associated with the use of the platinum group of catalysts [5–8]; the commercial catalysts, like the copper-chromium ($CuCr_2O_4$) and nickel catalysts, have found relatively little use [9–14]. However, even these studies have shown it possible to achieve a two-stage hydrogenation of furan aldehydes and ketones with the aid of $CuCr_2O_4$ and of nickel on kieselguhr (Ni_k), since in the presence of $CuCr_2O_4$ in certain temperature limits the furan ring is not touched.

Earlier [15] one of us had described the synthesis of the corresponding furan and tetrahydrofuran alcohols, 2-methyl-1,6-dioxaspiro (4,4) nonane and 2,7-dimethyl-1,6-dioxaspiro (4,4) nonane as the result of the two-stage reduction (using $CuCr_2O_4$ and Ni_k) of 3-(2'-methyl-5'-furyl)-2-propenal and 4-(2'-methyl-5'-furyl)-3-buten-2-one. In the same paper we discussed the problem of the structure of spirans of this type and the mechanism for their formation from furfurylidene ketones and γ-furylalkanols. Up to then the formation of similar spirans was established by various authors only in the hydrogenation of furylacrolein, furfurylideneacetone, difurfurylideneacetone and of the furan alcohols corresponding to them [9–11, 13, 16].

In this paper we communicate on the results obtained in the two-stage hydrogenation of a number of furfurylidene ketones, synthesized in 60-86 % yield by the condensation of furfural with the corresponding ketones, and specifically: furfurylidenemethyl ethyl ketone (I), furfurylidenemethyl propyl ketone (II), furfurylidenemethyl butyl ketone (III), furfurylidenemethyl amyl ketone (IV), furfurylidenemethyl isohexyl ketone (V), furfurylideneacetophenone (VI), furfurylidenepropiophenone (VII), and furfurylidenebenzylideneacetone (VIII).

Ketone (V) is new, while the other ketones have already been mentioned in the literature [17-20].

The hydrogenation of the indicated ketones in either anhydrous alcohol or dioxane (VI, VII) solution in the presence of $CuCr_2O_4$ at 120° and an initial hydrogen pressure of 90-150 atm. gave the corresponding furan alcohols (IX-XVI) in 60-78% yield; the latter under the same conditions with Ni_k are converted, in up to 75% yield, into the tetrahydrofuran alcohols (XVII-XXIV). In all cases (except VIII) it proved possible to isolate in from 3.5 to 13% yield the corresponding 1,6-dioxaspiro (4,4) nonane homologs (XXVII-XXXIII), formed as by-products in the last stage of the reaction, which can be explained by the following scheme:



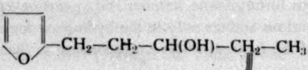
R=alkyl or H, R' =alkyl or aryl.

Data on the more important physical constants and analyses of all of the products obtained by the indicated procedure are given in Tables 1 and 2. * For comparison the literature data on 1,6-dioxaspiro (4,4) nonane and its 2-methyl homolog are also included in Table 2.

A regular change in the properties of the substances is observed in the respective homologous series. As can be seen, some depression of the molecular refraction is characteristic for the furan alcohols, which had already been mentioned earlier [20]. Optically, the homologs of 1,6-dioxaspirononane are normal. The furan and tetrahydrofuran secondary alcohols are liquids with a weak odor; the spirans are more mobile liquids than the alcohols, and have a specific terpene odor.

Simultaneously with hydrogenation of the furan ring, there occurs elimination of the carbonyl oxygen when (VI) and (VII) are hydrogenated under pressure in dioxane as the solvent, in the presence of Raney Ni catalyst (135-140°). The yield of (XXV) was 70 %, and that of (XXVI) was 42%. Apparently, such a hydrogenation course is characteristic for ketones of the type of furfurylideneacetophenone; the formation from the latter of 1-(α-tetrahydrofuryl)-3-phenylpropane (31% yield) was already described earlier [13], but under other hydrogenation conditions (Ni_k). The 1-(α-tetrahydrofuryl)-3-phenylpropane obtained by us is characterized by being more pure than the compound described by the indicated authors [13], as is demonstrated by the data given in Table 1.

We assumed a linear structure for the furan alcohols (IX), (X) and (XI), and consequently the corresponding structure of their derivatives is based on the following experimental data. Proceeding from β-(α-furyl) propionaldehyde [13] and C_2H_5MgBr we synthesized the alcohol



the normal structure of which is without dispute. This alcohol showed physical properties that were identical with those of alcohol (IX), obtained in the hydrogenation of furfurylidenemethyl ethyl ketone (Table 1). The 3,5-dinitrobenzoates, prepared from the two alcohols, had the same melting point. The mixed melting point was not depressed. In its physical properties the alcohol, synthesized in a similar manner from furylpropionaldehyde and C_4H_9MgBr, proved to be identical with (XI).

In addition, the iodoform reaction was applied to the tetrahydrofuran alcohols (XVII), (XVIII) and (XIX), giving a negative result, whereas when the same test was made on 1-(α-tetrahydrofuryl)-3-butanol, containing the CH(OH)–CH_3 grouping, a copious iodoform precipitate was obtained. This indicates that a similar grouping is absent in the indicated tetrahydrofuran alcohols, and consequently that both the starting furan alcohol (IX, X, XI) and the furfurylidene ketones (I, II, III) show a normal structure for the hydrocarbon chain.

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* Typographical errors appear in paper [25], Table 2 (for the boiling points given for products XXIX and XXXII).

TABLE 1

Constants of the Hydrogenation Products of Furfurylidene Ketones

	Hydrogenation product*	Boiling point	n_D^{20}	d_4^{20}	MR_D		Elementary composition (in %)				Starting substance, Catalyst	
					Found	Calculated	Found		Calculated			
							C	H	C	H		
(IX)	1-(α-f)-3-pentanol	120—123° (45 мм)	1.4759	1.006	43.22	43.79	70.37	8.91	70.10	9.15	(I)	$CuCr_2O_4$
(X)	1-(α-f)-3-hexanol	134—135 (45 мм)	1.4720	0.9831	47.92	48.41	71.33	9.42	71.39	9.59	(II)	
(XI)	1-(α-f)-3-heptanol	123—123.5 (6 мм)	1.4718	0.9706	52.56	53.03	72.51	10.15	72.43	9.88	(III)	
(XII)	1-(α-f)-3-octanol	129—130.5 (6 мм)	1.4710	0.9660	56.79	57.65	73.25	10.27	73.42	10.26	(IV)	
(XIII)	1-(α-f)-7-methyl-3-octanol	139—141 (7 мм)	1.4685	0.9499	61.66	62.27	74.32	10.73	74.24	10.54	(V)	
(XIV)	1-(α-f)-3-phenyl-3-propanol**	154—156 (7 мм)	1.5452	1.0998	58.16	58.66	77.08	7.15	77.20	6.98	(VI)	
(XV)	1-(α-f)-2-methyl-3-phenyl-3-propanol	159—160 (6 мм)	1.5423	1.0813	62.98	63.29	77.88	7.56	77.75	7.46	(VII)	
(XVI)	1-(α-f)-5-phenyl-3-pentanol	153—155 (2.5 мм)	1.5348	1.0494	68.60	67.90	77.93	7.72	78.26	7.83	(VIII)	
(XVII)	1-(α-thf)-3-pentanol	132—134 (45 мм)	1.4621	0.9717	44.77	44.73	68.38	11.41	68.33	11.47	(IX)	Nik
(XVIII)	1-(α-thf)-3-hexanol	151—154 (45 мм)	1.4595	0.9643	48.89	49.34	69.36	12.01	69.71	11.71	(X)	
(XIX)	1-(α-thf)-3-heptanol	125 (3 мм)	1.4582	0.9457	53.77	53.91	70.59	11.70	70.86	11.81	(XI)	
(XX)	1-(α-thf)-3-octanol	181—182.5 (46 мм)	1.4580	0.9357	58.28	58.58	72.07	12.15	71.95	12.07	(XII)	
(XXI)	1-(α-thf)-7-methyl-3-octanol	187—188 (43 мм)	1.4582	0.9291	62.97	63.20	73.03	12.41	72.83	12.23	(XIII)	
(XXII)	1-(α-thf)-3-phenyl-3-propanol***	176—178 (8 мм)	1.5294	1.0699	59.50	59.60	75.52	8.81	75.69	8.80	(XIV)	
(XXIII)	1-(α-thf)-2-methyl-3-phenyl-3-propanol	158—160 (4 мм)	1.5260	1.0566	64.00	64.22	76.45	8.80	76.32	9.15	(XV)	
(XXIV)	1-(α-thf)-5-phenyl-3-pentanol	165—170 (2.5 мм)	1.5192	1.0373	68.30	68.83	77.17	9.60	76.92	9.40	(XVI)	
(XXV)	1-(α-thf)-3-phenylpropane ****	124—126 (3 мм)	1.5140	0.9929	57.69	58.07	81.80	9.39	82.05	9.54	(VI)	Raney-Ni
(XXVI)	1-(α-thf)-2-methyl-3-phenylpropane	131—132 (3 мм)	1.5050	0.9708	62.42	62.70	81.60	9.46	82.30	9.87	(VII)	

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* f – furyl, thf – tetrahydrofuryl.

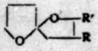
** Obtained earlier in 30% yield by the reduction of furfurylideneacetophenone with Na in alcohol [21]; b.p. 168-170° (12 mm), n_D^{20} 1.55, d_4^{20} 1.1.

*** Obtained earlier [5] in the hydrogenation of (VII) with platinum catalyst.

**** Obtained earlier [13] in the hydrogenation of furfurylideneacetophenone over Ni_k; b.p. 160° (28 mm), n_D^{25} 1.5200, d_4^{25} 0.9795 MR_D 59.01.

TABLE 2

Physical Constants of the Homologs of 1,6-Dioxaspiro(4,4)nonane of Type



Substance	Substituents		Boiling point	n_D^{20}	d_4^{20}	MR_D		Elementary composition (in %)		Hydrogenation product
	R′	R				Found	Calculated	Found	Calculated	
—	H	H	81—82° (60 мм)	1.4465 (25°)	1.0314 (25°)	33.12	33.41	—	—	*
—	CH_3	H	162—164	1.4428	0.9920	37.99	38.03	—	—	**
(XXVII)	C_2H_5	H	180—182.5	1.4464	0.9803	42.53	42.65	68.97, 9.95	69.19, 10.33	(IX)
(XXVIII)	C_3H_7	H	111—113 (45 мм)	1.4460	0.9601	47.22	47.27	70.45, 10.61	70.59, 10.59	(X)
(XXIX)	C_4H_9	H	130—133 (45 мм)	1.4481	0.9511	51.86	51.88	71.50, 11.13	71.64, 10.88	(XI)
(XXX)	C_5H_{11}	H	107.5—109 (20 мм)	1.4495	0.9410	56.58	56.50	72.31, 11.33	72.68, 11.18	(XII)
(XXXI)	iso-C_6H_{13}	H	112—114.5 (10 мм)	1.4500	0.9339	61.09	61.12	73.39, 11.56	73.53, 11.39	(XIII)
(XXXII)	C_6H_5	H	143—144 (7.5 мм)	1.5242	1.0884	57.44	57.52	76.80, 8.07	76.47, 7.9	(XIV)
(XXXIII)	C_6H_5	CH_3	128—130 (4 мм)	1.5173	1.0504	62.88	62.14	77.04, 8.73	77.03, 8.31	(XV)

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* Furylacrolein [13].

** Methylfurylacrolein [15].

Consequently, similar to benzaldehyde [22–24], furfural in alkaline medium condenses with methyl ethyl ketone and its alkyl homologs, mainly at the methyl group, and consequently the representations made by Kasiwagi [17] relative to the structure of furfurylidenemethyl ethyl ketone require a critical examination.

These considerations, expressed by us as early as 1953 [25], are in complete agreement with the later appearing experimental data of other authors, relating to the structure of furfurylidenemethyl butyl ketone and furfurylidenemethyl amyl ketone [26], and also furfurylidenemethyl ethyl ketone [27].

EXPERIMENTAL

Furfurylidene Ketones (I-V) were obtained by the condensation of furfural with the corresponding aliphatic ketones, taken in some excess. To an aqueous-alcohol solution of the reactant mixture with stirring was gradually added several milliliters of 10% NaOH solution. The reaction product separated as a yellow oil, which was separated, dried, and vacuum-distilled.

Previously unknown data for some of the physical constants of the indicated ketones are given below.

(I) B. P. 119–120° (12 mm), n_D^{20} 1.5808, d_4^{20} 1.066;

(II) B. P. 135–136° (15 mm), n_D^{20} 1,5592, d_4^{20} 1.026;

(III) B.P. 136–138° (11 mm), m. p. 41.5–42°, n_D^{42} 1.5434, d_4^{42} 1.0015;

(IV) B. P. 146–147° (8 mm), m. p. 43–44°

Furfurylidenemethyl isohexyl ketone (V) is a pale yellow liquid with characteristic odor.

B. P. 155.5–156° (7 mm), n_D^{20} 1.5370, d_4^{20} 0.9862.

Found %: C75.52; H 8.74 M 207.0. $C_{13}H_{18}O_2$. Calculated %: C75.69; H8.79. M 206.3.

The ketone forms the semicarbazone with m. p. 114° and the 2,4-dinitrophenylhydrazone with m.p. 132°.

Furfurylideneacetophenone (VI) and furfurylidenepropiophenone (VII) were obtained by the condensation of furfural with the corresponding ketones in anhydrous alcohol solution at 0° and the gradual addition of an alcoholic sodium ethylate solution.

Furfurylidenebenzylideneacetone (VIII) was obtained by the Claisen method [19].

Hydrogenation was accomplished by the typical method [15] in rotating steel autoclaves having volumes of 0.5 and 0.15 liter, respectively; electronic temperature regulators were used to maintain desired temperature; the catalysts used were Ni_k, a commercial catalyst of domestic manufacture, and $CuCr_2O_4$, which was prepared in the usual manner [28].

β-(α-Furyl) propionaldehyde was prepared by the Adkins method [13] in 52% yield. The compound is a pale yellow liquid.

B. P. 81–82° (17 mm), n_D^{20} 1.4766.

From the literature [29]: B. P. 81° (17 mm), n_D^{19} 1.4772.

1-(α-Furyl)-3-pentanol was obtained by the addition of 7.4 g of β-(α-furyl) propionaldehyde to C_2H_5MgBr, prepared from 1.44 g of Mg and 6.6 g of ethyl bromide in 30 ml of absolute ether. Vacuum-distillation gave 6.5 g (70.7%) of the compound.

B. P. 122–124° (45 mm), n_D^{20}1.4760, d_4^{20} 1.007, MR_D 43.19; Calculated 43.79.

Found %: C 69.87; H 9.32; OH 11.41. $C_9H_{14}O_2$. Calculated %: C 70.10; H9.15; OH 11.03.

The 3,5-dinitrobenzoate of the alcohol was obtained in the usual manner [30]; after two recrystallizations from alcohol the benzoate was obtained as yellow crystals with m. p. 83.5-84°.

Found %: N 8.34. $C_{16}H_{16}N_2O_7$. Calculated %: N 8.04.

The furan alcohol, obtained in the hydrogenation of furfurylidenemethyl ethyl ketone (IX) under the same conditions, gave the 3,5-dinitrobenzoate as yellow crystals with m. p. 83.5-84° (from alcohol).

Found %: N. 8.16. $C_{16}H_{16}N_2O_7$. Calculated %: N 8.04.

When a polarization microscope was used to compare the optical and other properties of the two 3,5-dinitrobenzoate specimens it was revealed that they could not be distinguished. Also, the mixed melting point of the two products was not depressed.

1-(α-Furyl)-3-heptanol was obtained in the same manner as the preceding by adding 6.2 g of β-(α-furyl) propionaldehyde to the Grignard reagent prepared from 1.2 g of magnesium turnings and 6.8 g of n-butyl bromide in 30 ml of absolute ether.

B. P. 121–122° (6 mm), n_D^{20} 1.4720, d_4^{20} 0.9704, MR_D 52.59; Calculated 53.03.

Found %: C 72.16; H 9.63; OH 9.30. $C_{11}H_{18}O_2$ Calculated %: C 72.43; H 9.88. OH 9.33.

The alcohol forms a liquid reaction product with phenyl isocyanate, which was not investigated further.

SUMMARY

1. The pressure hydrogenation in the presence of copperchromium catalyst of furfurylidenemethyl ethyl ketone, -methyl propyl ketone, -methyl butyl ketone, -methyl amyl ketone, -methyl isohexyl ketone, furfurylideneacetophenone, furfurylidenepropiophenone and furfurylidenebenzylideneacetone gave the corresponding furan alcohols in 60-78% yield. The latter when hydrogenated on nickel-on-kieselguhr were converted into the corresponding tetrahydrofuran alcohols in up to 75% yield. In this connection the alkyl and aryl homologs of 1,6-dioxaspiro(4,4)nonane were obtained as secondary reaction products. The properties of 23 new substances (V, IX-XIII, XV-XXI, XXIII, XXIV, XXVI-XXXIII) were described, and the constants of substances (XIV), (XXII) and (XXV), obtained by a new method, and also of the ketones (I), (II) and (III), were determined more accurately.

2. Experimental data were presented, showing that furfurylidene ketones of normal structure are formed when furfural is condensed with methyl alkyl ketones.

3. It was established that the hydrogenation under pressure of furfurylideneacetophenone and furfurylidenepropiophenone in the presence of Raney-Ni in dioxane solution gives as the main reaction product the corresponding tetrahydrofurylphenyl-alkanes.

LITERATURE CITED

[1] B. Wojcik, Ind. Eng. Chem. 40, 210 (948).

[2] A. A. Ponomarev and V. V. Zelenkova, Prog. Chem. 20, 589 (1951).

[3] A. A. Balandin and A. A. Ponomarev, Proc. Acad. Sci. USSR 100, 917 (1955).

[4] N. I. Shuikin, V. A. Tulupov and I. F. Belsky, J. Gen. Chem. 25, 1175 (1955) (T. p. 1125)*

[5] W. Kaufmann and R. Adams, J. Am. Chem. Soc. 45, 3029 (1923).

[6] G. Bargellini and E. Martegiani, Chem. Zentr., 1913, I, 296.

---

* T.p. = C. B. Translation pagination.

[7] K. Alder and C. Schmidt, C. A. 37,4702 (1943).

[8] H. Thoms and K. Soltner, Chem. Zentr. 1930, I, 2730.

[9] K. Alexander and L. Hafner, J. Am. Chem. Soc. 72,5506 (1950).

[10] K. Alexander and G. Smith, J. Am. Chem. Soc. 71,735 (1949).

[11] A. Hinz, G. Meyer and G. Schucking, Ber. 76,676 (1943).

[12] H. Wienhaus and H. Leonhardi, Chem. Zentr., 1930, I, 224.

[13] H. Burdick and H. Adkins, J. Am. Chem. Soc. 56, 438 (1934).

[14] R. Kleen, J. Am. Chem. Soc. 63, 3539 (1941).

[15] A. A. Ponomarev, V. P. Afanasyev and N. I. Kurochkin, Proc. Acad. Sci. USSR 87, 983 (1952); J. Gen. Chem. 23, 1426 (1953) (T. p. 1493).*

[16] K. Alexander, L. Hafner and L. Schniepp, J. Am. Chem. Soc. 73, 2725 (1951).

[17] I. Kasiwagi, Bull. Chem. Soc. 1, 90 Japan (1926); 2, 310 (1927).

[18] F. Breusch and E. Ulusoy, C. A. 42, 5850 (1948).

[19] L. Claisen and A. Ponder, Ann. 223, 147 (1884).

[20] E. C. Hughes and J. R. Johnson, J. Am. Chem. Soc. 53, 739 (1931).

[21] F. W. Semmler, Ber. 42, 2355 (1909).

[22] C. Harries and G. Muller, Ber. 35, 466, (1902).

[23] C. Harries and P. Bromberger, Ber. 35, 3089 (1902).

[24] K. Auwers and H. Voss, Ber. 42, 4420 (1909).

[25] A. A. Ponomarev, Z. V. Til, I. A. Markushina and K. Sapunar, Proc. Acad. Sci. USSR 93, 297 (1953).

[26] F. Breusch and E. Ulusoy, C. A. 47, 7478 (1953).

[27] Midorikawa, Ref. J. No. 5, 7454 (1955).

[28] R. Connor, K. Folkers and H. Adkins, J. Am. Chem. Soc. 54, 1138 (1932).

[29] S. Sherlin, A. Berlin, et al, J. Gen. Chem. 8, 7 (1938).

[30] W. C. Johnson, et al, Organic Reagents for Organic Analysis** (Leningrad Press, 1948), p. 56.

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* T. p. = C. B. Translation pagination.

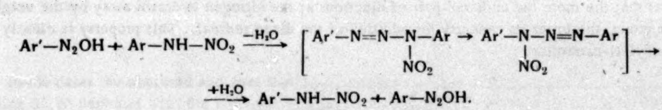
** In Russian.

STRUCTURE AND TRANSFORMATIONS OF N-NITROTRIAZENES

II. METHYLARYL-N-NITROTRIAZENES

N. M. Baranchik, I. V. Grachev and D. Z. Zavelsky

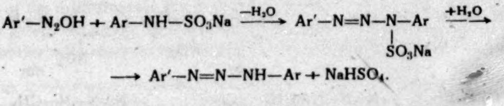
It was shown in the previous communication [1] that the condensation of active diazo compounds with phenylnitramine yields diaryl-N-nitrotriazenes, so unstable under the reaction conditions that they cannot be isolated in a pure state. A study of the decomposition products of the diaryl-N-nitrotriazenes revealed that they always contain a new N-nitramine, into whose composition enter the aryl part of the starting diazo compound and the diazobenzene, obtained from the starting phenyl-N-nitramine. Such an unexpected diazoamino condensation result was explained by the migration of the N-nitro group in the triazene chain of the formed diaryl-N-nitrotriazenes from one terminal nitrogen to another:



$$Ar'{-}N_2OH + Ar{-}NH{-}NO_2 \xrightarrow{-H_2O} \left[Ar'{-}N{=}N{-}\underset{NO_2}{\underset{|}{N}}{-}Ar \rightarrow Ar'{-}\underset{NO_2}{\underset{|}{N}}{-}N{=}N{-}Ar \right] \longrightarrow$$

$$\xrightarrow{+H_2O} Ar'{-}NH{-}NO_2 + Ar{-}N_2OH.$$

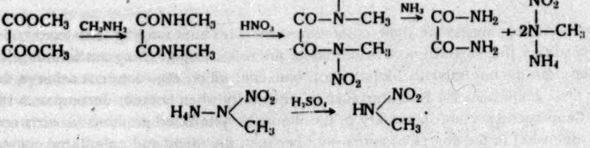
With the purpose in mind of obtaining some N-nitrotriazenes, and being convinced that the diaryl-N-nitrotriazenes are slightly too labile, we undertook the condensation of diazo compounds with methyl-N-nitramine, so as to obtain more stable methylaryl-N-nitrotriazenes. The assumption of a greater stability for the methylaryl-N-nitrotriazenes when compared with the diaryl-N-nitrotriazenes was based on the work done by one of us [2], which showed that the methylaryl-N-sulfotriazenes are so stable that they can be isolated in the pure state and kept, whereas the diaryl-N-sulfotriazenes decompose immediately after their formation with the liberation of diaryltriazenes and bisulfate:



$$Ar'{-}N_2OH + Ar{-}NH{-}SO_3Na \xrightarrow{-H_2O} Ar'{-}N{=}N{-}\underset{SO_3Na}{\underset{|}{N}}{-}Ar \xrightarrow{+H_2O}$$

$$\longrightarrow Ar'{-}N{=}N{-}NH{-}Ar + NaHSO_4.$$

Methyl-N-nitramine was synthesized from dimethyl oxalate by the Franchimont method [3]:

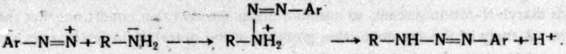


$$\begin{array}{c}COOCH_3\\|\\COOCH_3\end{array} \xrightarrow{CH_3NH_2} \begin{array}{c}CONHCH_3\\|\\CONHCH_3\end{array} \xrightarrow{HNO_3} \begin{array}{l}CO{-}\overset{NO_2}{\overset{|}{N}}{-}CH_3\\|\\CO{-}\underset{NO_2}{\underset{|}{N}}{-}CH_3\end{array} \xrightarrow{NH_3} \begin{array}{c}CO{-}NH_2\\|\\CO{-}NH_2\end{array} + 2\overset{NO_2}{\overset{|}{\underset{NH_4}{\underset{|}{N}}}}{-}CH_3$$

$$H_4N{-}N\begin{array}{l}\diagup NO_2\\ \diagdown CH_3\end{array} \xrightarrow{H_2SO_4} HN\begin{array}{l}\diagup NO_2\\ \diagdown CH_3\end{array}.$$

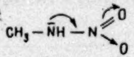
A description of this synthesis is given in EXPERIMENTAL, since it contains some details that are absent in the studies of Franchimont.

Methyl-N-nitramine in the form of its sodium salt was condensed with the diazo compounds in water solution. As was revealed, only active diazo compounds, containing electrophilic substituents in the benzene nucleus, enter into this reaction, since methylnitramine is more of a weak acid than a weak base. Actually, as is known [4], methylnitramine has the ionization constant $K_{0^\circ} = 3.0 \cdot 10^{-7}$ and $K_{25^\circ} = 7.2{:}10^{-7}$, which is extremely close to the ionization constant of carbonic acid ($K_{25^\circ} = 4.31 \cdot 10^{-7}$), and consequently readily forms salts, even with ammonia. The observed low activity shown by methylnitramine for diazoamino condensation is in good agreement with the representations of B. A. Porai-Koshits [5], who believes that the first stage in the acylation or diazoamino condensation of an amine is the addition of a positively charged acyl or diazo radical to an unshared electron pair of the amino nitrogen with the subsequent cleavage of water from the addition product:

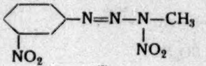


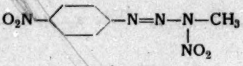
$$\mathrm{Ar{-}N{=}\overset{+}{N} + R{-}\overset{-}{N}H_2 \longrightarrow R{-}\underset{}{\overset{N=N-Ar}{\overset{|}{\overset{+}{N}H_2}}} \longrightarrow R{-}NH{-}N{=}N{-}Ar + H^+}.$$

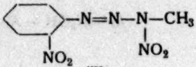
It is natural that the more the unshared pair of electrons at the nitrogen is drawn away by the neighboring electrophilic group, the lower its capacity for addition of the diazo radical. This property is clearly expressed for methyl-N-nitramine.

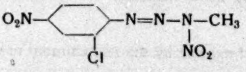


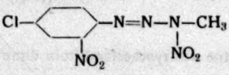
We condensed the methylnitramine with the diazo compounds obtained from 2-nitroaniline, 3-nitroaniline, 4-nitroaniline, 2-chloro-4-nitroaniline and 4-chloro-2-nitroaniline. For the first four diazo compounds the pH of the medium during condensation was maintained within the limits of 6 to 4.5, and for the last compound, as being more prone to migrate into the inactive form, in the pH range 3.5-3.8.


(I)


(II)

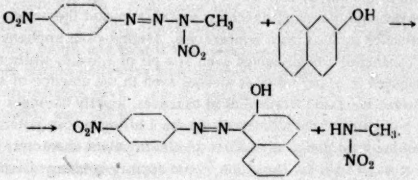

(III)


(IV)


(V)

The methylaryl-N-nitrotriazenes are light-colored powders with hues ranging from sand and slightly pink to brown, and showing a fine crystalline structure under the microscope. They are insoluble in water. Their recrystallization from organic solvents like alcohol, benzene, ether, etc. does not achieve the desired purpose, since under these conditions the N-nitrotriazenes, especially when heated, decompose with the liberation of a gas. Consequently, it was necessary to use the unrecrystallized products for elementary analysis, which was reflected somewhat in the degree of agreement between the found and calculated content of the elements. However, the obtained results, the same as the data of the other methods given below for the analysis of N-nitrotriazenes, do not leave any doubt as to the validity of the proposed structural formulas.

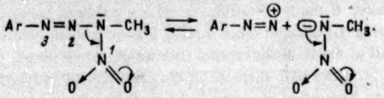
The methylaryl-N-triazenes behave like true diazoamino compounds: when dissolved and heated in glacial acetic acid, containing a small amount of α-naphthylamine, they give a bright color due to cleavage into the original components, the diazo part of which then couples with α-naphthylamine to give the corresponding azo dye [6]. The stability of the methylaryl-N-nitrotriazenes toward storage is small and strongly depends on their structure. If the N-nitrotriazene (I) is capable of being stored for a week with hardly any change, then its analog (II) changes more rapidly than in a week, while the triazene (V) is converted into a tar even after 3 days. All of the N-nitrotriazenes lose weight when stored, gradually evolving a gas. In this case also the instability increases with increase in the electrophilic properties of the substituents in the aryl nucleus of the triazenes. An interesting property of the methylaryltriazenes is their ability to enter into azo-coupling with β-naphthol in alcohol solution in the absence of any externally added acid. The reaction proceeds by the following scheme:



In all cases the obtained azo dyes showed a complete identity with the dyes formed by the direct coupling of β-naphthol with the corresponding diazo compounds. Simultaneous with the azo-coupling, the formation of methylnitramine was shown by its isolation from the reaction solution, remaining after removal of the azo dye, by extraction with ether and its identification with the authentic methylnitramine.

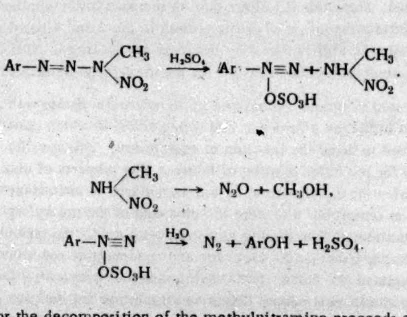
To quantitatively study the azo-coupling reaction each of the nitrotriazenes was added to an alcohol solution of β-naphthol, and after standing for a day, the excess β-naphthol was determined by titration with p-nitrophenyldiazonium chloride solution, while the methylnitramine was determined by potentiometric titration with sodium hydroxide solution. It was found that for the nitrotriazene (I) from 3-nitrodiazobenzene the coupling goes to the extent of 95-96%, for the nitrotriazenes (II) and (III) from 4-nitro- and 2-nitrodiazobenzenes to the extent of 93.6-94.8%, for (IV) from 4-nitro-2-chlorodiazobenzene to the extent of 77-79%, and for (V) from 4-chloro-2-nitrodiazobenzene only to the extent of 69-72%, even after supplementary boiling of the reaction solution of 3 hours. From this it follows that an increase in the number of electrophilic groups in the benzene rings of the nitrotriazenes and their being present in the 2 and 4 positions, especially in the 2 position for the nitro group, reduce the ability shown by triazenes for cleavage. This conclusion is found to be in accord with the similar rules observed by one of us [7] for the methylaryl-N-sulfotriazene series.

As is known, the trisubstituted triazenes synthesized up to now were always stable in neutral medium and suffered cleavage only under the influence of more or less strong acids, in which connection an elevated temperature was frequently needed to drive the reaction to completion. This specific property of the triazenes was successfully used in industry for the color printing of fabrics. The property of cleaving the diazo part in the absence of acid was revealed for the first time by the methylaryl-N-nitrotriazenes that we had synthesized. However, it is necessary to remember that here the cleavage of the methylaryl-N-nitrotriazenes yields the free methylnitramine, which although functioning as a very weak acid, still undoubtedly catalyzes further cleavage until a definite equilibrium between the cleavage and condensation reactions is attained. In alcohol solution in the presence of β-naphthol the diazo part being cleaved, irreversibly forming the azo dye, escapes from the reaction sphere and in this manner drives to completion the reaction for the cleavage of the nitrotriazenes obtained from mononitrodiazobenzenes. As regards the nitrotriazenes derived from the nitrochlorodiazobenzenes, then their cleavage proceeds not only more slowly due to the additional electrophilic groups present, but also not quantitatively, apparently due to the progress of secondary reactions, which were not studied by us more closely. The unusual ability shown by N-nitrotriazenes to cleave in the absence of acids can be explained by the fact that the nitro group, linked to the 1 nitrogen in the triazene chain, so strongly attracts the electrons of the bond, common to both the 1 and 2 nitrogen atoms, as to make impossible the rupture of this bond with the formation of ions in accord with the following scheme:



The following comparisons of the ability shown by certain acyltriazenes to cleave are of interest. According to Dimroth [8], methylphenyl-N-acetyltriazene is so stable toward the action of acids that 1N hydrochloric acid is without influence on it at room temperature. Methyl-(4-nitrophenyl)-N-sulfotriazene [7] at the same temperature is capable of being cleaved even at a pH of 3.5-4.0, while methyl-(4-nitrophenyl)-N-nitrotriazene is gradually cleaved in either water or alcohol even in the absence of acid. From this it can be concluded that the bond between the 1 and 2 nitrogens in triazenes, usually having a covalent character, depending on the electrophilic properties of the substituents on the 1 nitrogen, can polarize to such an extent that in the case, for example, of the nitro group, it acquires an electrovalent character, since it is capable of decomposing in either alcohol or water with the formation of two oppositely charged ions.

In the quantitative analysis for diazo nitrogen in N-nitrotriazenes by the usual method of boiling the triazene sample in dilute up to 68% sulfuric acid there is liberated, besides one molecule of diazo nitrogen, also a molecule of nitrous oxide. This fact is easily explained, since nitramines, and in particular methylnitramine, are capable of cleaving nitrous oxide under the influence of sulfuric acid [9]. A more detailed study of the cleavage reaction of N-nitrotriazenes revealed that the liberation of nitrous oxide proceeds at a much faster rate than does the liberation of nitrogen. Actually, in the case of methyl-(3'-nitrophenyl)-N-nitrotriazene the first half of the gas evolved in the experiment has d 1.814, and the second half has d 1.390, while in the case of methyl-(2'-nitrophenyl)-N-nitrotriazene the corresponding values are d 1.936 and d 1.270 (dN_2O 1.9774 and dN_2 1.2505). From this it follows that the decomposition of nitrotriazenes in sulfuric acid proceeds in stepwise fashion by the following scheme:



$$\mathrm{Ar{-}N{=}N{-}N}\begin{matrix}\mathrm{CH_3}\\ \mathrm{NO_2}\end{matrix} \xrightarrow{H_2SO_4} \underset{\mathrm{OSO_3H}}{\mathrm{Ar{-}N}}{\equiv}\mathrm{N} + \mathrm{NH}\begin{matrix}\mathrm{CH_3}\\ \mathrm{NO_2}\end{matrix}.$$

$$\mathrm{NH}\begin{matrix}\mathrm{CH_3}\\ \mathrm{NO_2}\end{matrix} \longrightarrow N_2O + CH_3OH,$$

$$\underset{\mathrm{OSO_3H}}{\mathrm{Ar{-}N}}{\equiv}\mathrm{N} \xrightarrow{H_2O} N_2 + ArOH + H_2SO_4.$$

Here reaction (2) for the decomposition of the methylnitramine proceeds at a much faster than does reaction (3) for the decomposition of the diazo compound. In turn, reaction (3) proceeds more slowly the more electrophilic the substituent in the benzene ring of the diazo compound and the more of these substituents present. The last circumstance was additionally verified by us by means of some special experiments made on the decomposition of 3-nitrodiazobenzene, 2-nitrodiazobenzene and 4-nitro-2-chlorodiazobenzene. It is in full agreement with the known data [10] on the comparative stability of the diazo groups found in differently substituted diazo compounds.

EXPERIMENTAL

I. Synthesis of Methyl-N-nitramine

Dimethyloxamide [11]. 59 g of dimethyl oxalate, synthesized in known manner [12], was added in small portions with rapid stirring to a flask, containing 200 ml of 11% aqueous methylamine solution, and cooled externally with cold water. Fine white crystals of dimethyloxamide deposited almost immediately. On conclusion of adding the ester the reaction mass was allowed to stand for several hours to complete the crystallization, then it was filtered, washed with a small amount of ice water, pressed, and dried. Recrystallization from alcohol gave snow-white needles with m. p. 216-217°. Yield 70-75%.

Dinitrodimethyloxamide [3]. To a flask containing 30 ml of 98% nitric acid was added in small portions with either shaking or stirring 5.8 g of dry dimethyloxamide. When the latter had dissolved the reaction mass was allowed to stand for 1-2 hours, and then it was poured into 400 ml of cold water. The obtained white crystals of water-insoluble dinitro derivative were separated and washed with water to remove nitric acid. Two recrystallizations from alcohol gave a product with m. p. 123-124° [3]. The yield of dinitrodimethyloxamide before recrystallization was ~98%.

Methylnitramine [11]. With stirring and cooling 87 g of dinitrodimethyloxamide was added in small portions in 2 hours to a flask, containing 250-270 ml of aqueous (22%) ammonia. Then the water-insoluble oxamide, formed as the result of reaction, was filtered from the reaction mass. The colorless filtrate, composed of the ammonium salt of methylnitramine and excess ammonia, was evaporated on the water bath to the disappearance of ammonia odor, and then with external ice-cooling and rapid stirring it was slowly acidified with 5-10% sulfuric acid to pH 3 (the appearance of a violet stain on Congo paper). To avoid decomposition of the methylnitramine the acidified solution was immediately extracted with several 100-150 ml portions of ether. Removal of the ether by distillation gave colorless crystals of the methylnitramine, after separation and drying, with m. p. 37-38°. Yield 85-90%.

II. Condensation of Diazo Compounds With Methyl-N-nitramine

1. 1-Methyl-1-nitro-3-(3'-nitrophenyl) triazene (I). A solution of 3-nitrophenyldiazonium chloride was prepared by diazotizing 0.01 mole of 3-nitroaniline with nitrite in the presence of 0.03 mole of hydrochloric acid as a 4N solution. One gram of methylnitramine was dissolved in a slight excess of sodium hydroxide solution. To the methyinitraminate solution was added a concentrated buffer solution of a mixture of sodium acetate and acetic acid with pH 6, and then the diazonium chloride solution was added at room temperature with vigorous stirring. Here the reaction mass quickly acquired a milk-white turbidity, gradually changing to a light flocculent precipitate the amount of which rapidly increased. The condensation is accompanied by the liberation of acid, which had to be constantly neutralized with either sodium acetate or bicarbonate in order to maintain the pH of the medium at ≈ 6. (Indicator papers were used to control the pH). Two hours after starting the reaction the reaction mass was filtered. The precipitate was washed to the disappearance of free diazo compound in the wash water (test with a solution of H-acid) and then it was dried at room temperature in a vacuum-desiccator. The yield of nitrotriazene (based on the starting diazo compound) was 87-90 %. The N-nitrotriazene synthesized in this manner represents a light, finely crystalline powder with a light-pink cast. We were unable to recrystallize the compound, since it is insoluble in water, while in organic solvents like alcohol, benzene, ether, etc. it decomposes with the liberation of a gas, especially when heated. When we attempted to determine its melting point the nitrotriazene flashed even before the melting point was reached. When heated in glacial acetic acid, containing a small amount of α-naphthylamine, a bright color appears due to cleavage of the nitrotriazene with the liberation of the diazo compound, forming an azo dye with the α-naphthylamine. When stored the nitrotriazene slowly liberates a gas, loses weight, gradually darkens, and finally is transformed into a black viscous tarry substance. When stored for 2 months the product loses about 28 % of its weight. The elementary analysis was run on the freshly synthesized, but not recrystallized product.

Found %: C 38.13; H 3.38; N 31.35. $C_7H_7O_4N_5$. Calculated %: C 37.33; H. 3.13; N 31.11.

2. 1-Methyl-1-nitro-3-(4'-nitrophenyl) triazene (II). A solution of 4-nitrophenyldiazonium chloride, prepared from 0.01 mole of 4-nitroaniline and 0.03 mole of hydrochloric acid, was added at room temperature and with stirring to a solution of sodium methyl-N-nitraminate, buffered with a mixture of sodium acetate and acetic acid. During the condensation the pH of the reaction mass was kept within the limits 5.0-5.5. The deposition of a light-yellow flocculent precipitate began immediately and was complete in 2-3 hours after mixing the components. The precipitate was filtered, washed from traces of the diazo compounds, pressed, and vacuum-dried. The yield of the triazene (based on the diazo compound) was ≈ 70 %. The substance was obtained as a finely crystalline light-yellow powder, which flashed when heated, was insoluble in water, and did not lend itself to recrystallization from organic solvents due to decomposition. It also gives the bright color characteristic for triazenes when its solution in glacial acetic acid is heated in the presence of α-naphthylamine. The triazene from 4-nitrodiazobenzene is even less stable to storage than the above described triazene from 3-nitrodiazobenzene. After 12-15 days it is converted into a tar, and in a month it loses 31.0% in weight.

Found %: C 38.25; H 3.58; N 31.60. $C_7H_7O_4N_5$. Calculated %: C 37.33. H 3.13; N 31.11.

3. 1-Methyl-1-nitro-3-(2'-nitrophenyl) triazene (III). The condensation of 2-nitrophenyldiazonium chloride with methyl-N-nitramine was run under the conditions described above, but at pH 4.8-5.0. The yield of the triazene was 55-60%. The substance was obtained as a powder with a light-sand color, rapidly assuming a dark-brown color in the air and going to a tar. For the remainder it is close in its properties to the above-described triazenes. After storage for 20 days it lost 31-33% of its weight.

Found %: C 38.07; H 3.50; N 31.54. $C_7H_7O_4N_5$. Calculated %: C 37.33; H 3.13; N 31.11.

4. 1-Methyl-1-nitro-3- (4'-nitro-2'-chlorophenyl) triazene (IV). The condensation of 4-nitro-2-chlorophenyldiazonium chloride was run with a 50% excess of methyl-N-nitramine at pH 4.5-5.0. The yield of the triazene was about 55%. The triazene was obtained as a powder with a light-sand color, turning to a tar when stored and losing 20.8% of its weight in a month.

Found %: C 33.02; H 2.54; Cl 12.84. $C_7H_6O_4N_5Cl$. Calculated %: C 32.40; H 2.32; Cl 13.70.

5. 1-Methyl-1-nitro-3-(4'-chloro-2'-nitrophenyl) triazene (V). The diazotization of 0.01 mole of 4-chloro-2-nitroaniline was done in the presence of 0.05 mole of hydrochloric acid. To the acid solution, rapidly at first, and then slowly, was added a 3-3.5-fold excess of sodium methylnitraminate solution. The latter was prepared by dissolving 3 g of methylnitramine in an equivalent amount of 2N sodium hydroxide solution. When a permanent white turbidity (at pH 3.8) appeared in the reaction mixture the addition of the sodium methylnitraminate was terminated, and stirring was continued for another 1.5-2.0 hours. A flocculent precipitate accumulated during this time, and the pH of the medium dropped to 2.8-3.0. The precipitate was filtered, washed from unreacted diazo compound, and vacuum-dried. The yield was about 30%. The triazene was obtained as a light-brown powder, showing rapid darkening when stored, and changing to a tar more rapidly than all of the above described triazenes (in approximately 3 days). The weight loss in this time was 8%.

Found %: C 33.43; Cl 13.6. $C_7H_6O_4N_5Cl$. Calculated %: C 32.40; Cl 13.70.

III. Cleavage of N-Nitrotriazenes Into Original Components

A suspension of 1-methyl-1-nitro-3-(4'-nitrophenyl) triazene in water was stirred for 3 hours. When poured into an alkaline solution of β-naphthol or a soda-alkaline solution of H-acid the filtrate from this suspension gave a weak color of the azo dye, identical with that obtained by the direct coupling of 4-nitrodiazobenzene with the enumerated azo-components. The other methylaryl-N-nitrotriazenes behave in a similar manner. 1-Methyl-1-nitro-3-(4'-nitrophenyl) triazene was dissolved in cold alcohol. When poured into an alcohol solution of β-naphthol the obtained solution gave a color, characteristic for 4-nitro-phenylazoβ-naphthol. An alcohol solution of the nitrotriazene on standing turned yellow and acquired the odor of nitrobenzene and acetaldehyde.

Quantitative Determination of the Cleavage of N-Nitrotriazenes in Alcohol

The weighed sample of the nitrotriazene (~ 0.001 mole) was dissolved in 20 ml of a 0.1 N alcohol solution of β-naphthol at room temperature. After standing 1 day the solution was diluted with water, buffer solution was added (up to a pH of 6 or 7), and the excess β-naphthol was titrated with a 0.1N solution of p-nitrophenyldiazonium chloride.

The diazo compounds, cleaved from the methylaryl-N-nitrotriazenes in alcohol solution by β-naphthol, were identified as follows: a sample of the N-nitrotriazene was kept in an alcohol solution of β-naphthol at room temperature for several hours, then the solution was diluted with water, filtered, and the deposited azo dye washed and its melting point determined.

Under these conditions the N-nitrotriazene from 3-nitro-diazobenzene formed a dye with m. p. 194-195°. Its mixture with the specially synthesized 3-nitrophenylazo-β-naphthol, melting at 194.5-195.5° [14], failed to depress the melting point.

The dye, obtained from the N-nitrotriazene that was synthesized from 2-nitrodiazobenzene, was identified in exactly the same manner. Its m. p. was 211-212°, and its mixed melting point with the authentic 2-nitrophenylazo-β-naphthol, melting at 212° [14], also was not depressed.

The presence of the second component, found in the composition of the N-nitrotriazene, was shown as follows. After standing for several hours, a solution of the N-nitrotriazene in alcohol, containing β-naphthol, was strongly diluted with water and the azo dye filtered. To purify it the colored mother liquor was boiled with activated charcoal, acidified, and extracted with ether. Removal of the ether by distillation gave a substance with m. p. 35-36°, the mixture of which with authentic methyl-N-nitramine, having m. p. 37-38°, melted at 36-38°.

To quantitatively determine the methyl-N-nitramine a sample of 0.2250 g of 1-methyl-1-nitro-3-(2'-nitrophenyl) triazene was dissolved in alcohol, containing an equivalent amount of β-naphthol. After several hours the solution was diluted with water, the deposited azo dye filtered, and the mother liquor titrated potentiometrically with 0.1N sodium hydroxide solution, using a pH meter with glass electrode. 9.8 ml of 0.1N sodium hydroxide was consumed in the titration, which corresponds to 98% methylnitramine.

IV. Decomposition of N-Nitrotriazenes in Sulfuric Acid

The determination of diazo nitrogen, evolved quantitatively when diazoamino compounds are boiled in dilute sulfuric acid, was run as follows for the N-nitrotriazenes: a weighed sample of the triazene was placed in a 150-ml round-bottomed flask, fitted with a dropping funnel containing 68% sulfuric acid, and connected, on the one hand, to a source of pure carbon dioxide(Kipp apparatus), and on the other—to a gas burette, filled with 50% potassium hydroxide solution. Carbon dioxide was passed through the flask until all of the air had been displaced, then the flask was cooled with ice and 40-50 ml of 68% sulfuric acid was added to it from the dropping funnel. All of the gas, formed from the decomposition of the heated solution of the triazene in sulfuric acid, through which carbon dioxide was passed, was collected in the gas burette over alkali and measured. The determination results are given in Table 2.

From the data in Table 2 it can be seen that not 1, but 2 moles of gas are liberated from 1 mole of the N-nitrotriazene.

The specific gravity of the gas was determined as follows. A sample of the N-nitrotriazene (about 0.7 g) was decomposed with 68% sulfuric acid by the above described method. In two experiments, where the decomposition rate was regulated by the degree of heating, the gas, in measure with its formation, was collected in the gas burette in two portions. Here the 1st and 2nd halves of the gas were transferred separately from the gas burette to an evacuated and weighed gas pycnometer (capacity 69.56 ml) and the contained gas was weighed at known temperatures and pressures. In the third experiment the gas, obtained from one-half the amount of triazene, was collected together and its average specific gravity was determined in the same

TABLE 1

Determination of the Diazo Components in Alcohol Solutions of Nitrotriazenes and β-Naphthol

Diazo component present in the triazene	Weight of triazene (g)	Amount 0.1N β-naphthol used for coupling (ml)	Found diazo (in %)
3- Nitrodiazobenzene	0.2254 0.2255	9.50 9.60	94.9 95.9
4- Nitrodiazobenzene	0.2262 0.2256	9.40 9.50	93.6 94.8
2- Nitrodiazobenzene	0.2244	9.40	94.3
4- Nitro-2-chloro-diazobenzene	0.2712 0.2616	8.25 7.77	79.0 77.1
4- Chloro-2-nitro-diazobenzene*	0.2590 0.1940	6.90 5.36	69.2 71.7

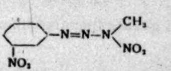
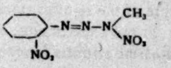
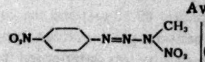
TABLE 2

Determination of the Diazo Nitrogen in N-Nitrotriazenes

No. of analyzed triazene	Weight (g)	Amount gas evolved (ml)	Reaction conditions (temp., pressure)	Found gas (in wt. %), based on		Calculated amount gas (in %), based on		
				N_2	$N_2 + N_2O$	1 mole N_2	2 mole N_2	N_2+1 mole N_2O
(III)	0.0668 0.0640 0.0692	14.9 13.8 14.7	22°; 751.7 24, 770.3 22, 777.8	24.96 24.51 24.62	32.21 31.63 31.77	12.44	24.88	31.99
(II)	0.0486 0.0458 0.0657	10.6 10.0 14.4	18.3° 749 18, 749 20, 747.6	24.74 24.80 24.62	31.94 32.01 31.78	12.44	24.88	31.99
(I)	0.0766 0.0656	16.7 14.2	21°, 766.6 20, 765.2	25.01 24.90	32.27 32.14	12.44	24.88	31.99
(IV)	0.0772	10.0	21°, 736.3	14.26	18.40	10.79	21.58	27.74

TABLE 3

Determination of the Specific Gravity of the Gas Formed in the Decomposition of Nitrotriazenes in 68% Sulfuric Acid

Formula of analyzed substance	1st gas portion			2nd gas portion		
	reaction cond.	Weight of gas (g)	Sp. grav. of gas (g/liter)	Reaction cond.	Weight of gas (g)	Sp. grav. of gas (g/liter)
	22° (773.7 мм)	0.1162	1.814	21° (772.5 мм)	0.0894	1.390
	22° (748.6 мм)	0.1200	1.936	23° (749.0 мм)	0.0784 **	1.270
Average sample of the total gas						
	20° (762.8 мм)	0.1042	1.633			

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* Boiled under reflux for 3 hours after standing for 24 hours.

** The 2nd gas portion is liberated in the course of boiling for 4-5 hours.

manner as before. The obtained results are summarized in Table 3.

Taking the specific gravity of pure N_2 as 1.2505, of N_2O as 1.9774, and of their equimolar mixture as 1.614, it can be concluded that the gas first liberated in the decomposition of the methylaryltriazenes is mainly nitrous oxide, and then nitrogen toward the end. This tendency is more clearly defined for the nitrotriazene from 2-nitrodiazobenzene than for its analog from 3-nitrodiazobenzene. The specific gravity of the average sample from the total gas supports the fact that the latter is composed of nearly equal amounts of nitrogen and nitrous oxide.

SUMMARY

1. The condensation of diazo compounds with N-methylnitramine gave a new series of N-nitrotriazenes. Since the N-methylnitramine is a very weak base, only active diazo compounds are capable of condensing with it.

2. The methylaryl-N-nitrotriazenes, in contrast to previously known triazenes, are capable of coupling with β-naphthol in alcohol solution in the absence of acid. This phenomenon is explained by the strongly electrophilic character of the nitro group linked to the nitrogen of the triazene chain.

3. Besides the liberation of diazo nitrogen, the heating of methylaryl-N-nitrotriazenes in dilute sulfuric acid also results in the liberation of nitrous oxide. The latter is formed as the decomposition result of the cleaved methylnitramine; in this connection the indicated reaction proceeds at a faster rate than does the decomposition of the diazo compound.

4. The cleavage of the methylaryl-N-nitrotriazenes into their basic components becomes more difficult the more electrophilic the substituents in the benzene ring and the greater their number.

LITERATURE CITED

[1] N. M. Baranchik, I. V. Grachev and D. Z. Zavelsky, J. Gen. Chem. 23, 1572 (1953).[*]

[2] D. Z. Zavelsky, Collection Reminiscences of A. E. Porai-Koshits (State Chemical Press, 1949), p. 247.[**]

[3] Franchimont and Klobbie, Rec. trav. chim. 7, 343 (1888); Franchimont, Rec. trav. chim 13, 308 (1894).

[4] Franchimont and Klobbie, Rec. trav. chim. 7, 354 (1888).

[5] B. A. Porai-Koshits, Collection Reminiscences of A. E. Porai-Koshits (State Chemical Press, 1949), p. 223.[**]

[6] E. Bamberger, Ber. 28, 839 (1895).

[7] D. Z. Zavelsky and L. A. Lishnevskaya, J. Gen. Chem. Suppl. I, 446 (1953).

[8] O. Dimroth, Ber. 38, 670 (1905).

[9] Franchimont, Rec. trav. chim. 17, 288 (1898); van Erp, Rec. trav. Chim., 14, 1 (1895).

[10] K. Saunders, Aromatic Diazo Compounds and Their Technical Application (State United Science and Technology Press, 1935), p. 90.[**]

[11] Wallach and Boehringer, Ann. 184, 51 (1877).

[12] Organic Syntheses, Coll. Vol. II, p. 331 (1949).

[13] Franchimont and Klobbie, Rec. trav. chim. 8, 295 (1889).

[14] A. Brunner, Analysis of Azo Dyes (State Chemical Press, 1933), p. 93.[**]

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[*] Original Russian pagination. See C. B. translation.

[**] In Russian.

INVESTIGATIONS ON IMIDAZOLE DERIVATIVES

XV. NITRATION OF BENZIMIDAZOLONE AND OF 1,3-DIMETHYLBENZIMIDAZOLONE

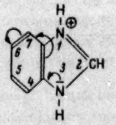
L. S. Efros and A. V. Eltsov

Several investigators have studied the nitration of benzimidazole and its derivatives; it has been suggested that in this reaction benzimidazole derivatives function in the form of cations[1] (I); the latter contain the equivalent nitrogen atoms of the heterocycle whose unshared electron pairs activate the ortho- and para-positions of the benzene ring and thereby facilitate the entry of cationic substituents.

It has been established that under the influence of the imidazole grouping, the electron shell of the benzene ring of benzimidazole is deformed; its symmetry is destroyed, the double-bond character of the bond between the 4-5 and 6-7 carbon atoms being intensified. In such a molecule the directive effect of the nitrogen atoms of the heterocycle is transmitted along the chain of conjugated bonds and is most strongly manifested in the 5-and 6-positions which are the ends of the conjugated chain due to the bond between these atoms approximating to a single bond. Positions 5 and 6 are consequently considerably more reactive than positions 4 and 7 and resemble the α-position of naphthalene in their activity. Carbon-containing substituents in the 2-position have no substantial influence upon the direction of a cationic substitution reaction taking place in the 5- and 6 positions.

In the light of the foregoing considerations it was of interest to study the nitration of 2-hydroxybenzimidazole or benzimidazolone (II). Results of this study are described below.

Kym and Ratner [2] synthesized 5-nitrobenzimidazolone (III) from 1,2-diamino-4-nitrobenzene and urea and further nitrated it to 5,6-dinitrobenzimidazolone (IV). They were struck by the facility with which the second nitro group entered the 6-position. James and Turner [3] repeated the work of Kym and Ratner and found that a trinitro derivative can be readily prepared from 5-nitrobenzimidazolone. They assigned to this the structure of 4,5,6-trinitrobenzimidazolone (V).



(I)

In view of the lack of systematic investigations in this field, we started by studying the nitration of benzimidazolone (II) itself. Under very mild conditions (at 0° and with an equimolar amount of nitric acid) benzimidazolone (II), dissolved in concentrated sulfuric acid, readily forms 5-nitrobenzimidazolone (III) in good yield; it was identical with the product obtained by the method of Kym and Ratner from 1,2-diamino-4-nitrobenzene and urea [2]. We were unable to isolate 4-nitrobenzimidazolone (prepared by us from urea and 1,2-diamino-3-nitrobenzene) from the reaction products. This compound is evidently not formed in appreciable amount during direct nitration of benzimidazolone. This behavior is consistent with the above-described general properties of benzimidazoles.

Under the same conditions (but with the appropriate amount of nitric acid which may be in excess of the theoretical requirement) the benzimidazolone (II) also undergoes dinitration with formation of 5,6-dinitrobenzimidazolone (IV). This dinitro derivative is readily obtained under the same conditions from 5-nitrobenzimidazolone (III).

On attempting, however, to repeat the experiments of Kym and Ratner on the nitration of 5-nitrobenzimidazolone (III), which they carried out in excess fuming nitric acid at a temperature reaching 40°, we obtained a heterogeneous product differing in properties from 5,6-dinitrobenzimidazolone (IV). The mixture of substances that we obtained gave a dark-red product when shaken with an emulsion of aniline in water (5,6-dinitrobenzimidazolone (IV) does not possess this property), and the elementary analysis gave a nitrogen content higher than that calculated for a dinitro derivative. On repeating the experiment at 40-45° we obtained, from 5-nitrobenzimidazolone(IV), a product in 55 % yield which melted after recrystallization at 258° and corresponded in elementary composition to a trinitro derivative of benzimidazolone.

The same product is also obtained from benzimidazolone (II) when its solution is nitrated in concentrated sulfuric acid at 40°. The substance was identified as the vicinal trinitro derivative (V) since we prepared it from 5,6-dinitrobenzimidazolone (IV).

James and Turner [3] report a melting point above 300° for the trinitro derivative of benzimidazole that they prepared. Unfortunately it was difficult to repeat these authors' experiments since they do not state the temperatures of operation during nitration.

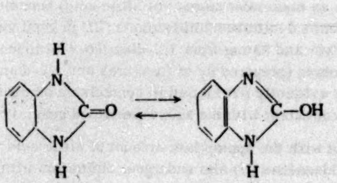
James and Turner [3] mention that their trinitro compound reacts with great facility with isopropylamine with formation of an isopropylaminodinitrobenzimidazolone, and that they performed the replacement of a nitro group by the p-chloroaniline residue under fairly drastic conditions (heating to 180° for 1 hour). Kym and Ratner [2] showed that under these conditions aniline also reacts with 5,6 -dinitrobenzimidazole (IV) with formation of the 5-phenylamino derivative.

In contrast to the above, our 4,5,6-trinitro derivative reacted with aniline in water by simple shaking in the cold to give a phenylaminodinitro derivative to which we assigned the structure of 5-(phenylamino)-4,6-dinitrobenzimidazole (XIV), taking into account the high lability of the nitro group in the 5-position under the influence of the two nitro groups in the ortho-position. The replacement of a nitro group by the aniline residue in this case and in the similar cases described below goes with excellent yield, and nitrous acid is formed. On acidification of the reaction mass, the excess of aniline is diazotized and the resultant diazo compound is detected by the coupling reaction with alkaline β -naphthol.

Under very mild conditions (in the cold) 4,5,6-trinitrobenzimidazolone (V) also reacts with p-chloroaniline to form 5-p-chlorophenylamino)-4,6-dinitrobenzimidazolone (XVI) which James and Turner obtained when performing the reaction at 180°.

The astonishing facility of entry of the third nitro group into the benzimidazolone molecule prompted us also to attempt the preparation of the vicinal tetranitro derivative (VI) by nitration of a solution of 4,5,6-trinitrobenzimidazolone (V) in monohydrate at 100°. Tetranitrobenzimidazolone (VI) was readily formed in 65 % yield. The latter readily gives the di-(phenylamino)-dinitro derivative (XV) when shaken with aniline in water in the cold.

Kym and Ratner [2] assumed that benzimidazolone enters into the nitration reaction in the tautomeric form of 2-hydroxybenzimidazole. The presence of the hydroxy group appeared to account for the ease of nitration, the steering of the reaction into the 5- and 6-positions being consistent with the properties of other derivatives of benzimidazole.



In order to check the correctness of this explanation, we studied the nitration of 1,3-dimethylbenzimidazolone (VII) which is not susceptible to tautomerism. 1,3-Dimethylbenzimidazolone (VII) was prepared by the action of dimethyl sulfate on an alkaline solution of benzimidazolone [4]. Nitration was found to go exactly as in the case of nitration of benzimidazolone.

The starting product (VII) readily gave 5-nitro-1,3-dimethylbenzimidazolone (VIII), which is identical with the product of methylation of 5-nitrobenzimidazolone. From (VIII) was synthesized the dinitro product (IX) whose structure was confirmed by preparation of the same substance by methylation of 5,6-dinitrobenzimidazolone.

With the same ease as trinitobenzimidazolone (V) and with equally good yield, 4,5,6-trinito-1,3-dimethylbenzimidazolone (X) was obtained from the dinitro product (IX). When shaken with aniline in water, (X) gave the bright-red phenylaminodinitro derivative (XII).

4,5,6,7-Tetranitro-1,3-dimethylbenzimidazolone (XI) is prepared in a similar manner to its non-methylated analog (VI) from the trinitro derivative (X), but this reaction is accompanied by partial oxidation of the methyl groups.

When treated in the cold with aniline in water, (XI) gives a bright-red precipitate corresponding in elementary composition to phenylaminotrinitrodimethylbenzimidazolone. Brief heating of the latter with aniline in water leads to replacement of the second nitro group by the aniline residue with formation of the di-(phenylamino)-dinitro derivative of 1,3-dimethylbenzimidazolone. Since the labilities of the nitro groups in the 5- and 6-positions of tetranitrobenzimidazolone (VI) and in 1,3-dimethyltetranitrobenzimidazolone (XI) must be identical, it can be assumed that stepwise introduction of phenylamino groups into the latter is associated with the steric hindrance induced by the methyl groups during substitution of nitro groups in positions 4 and 7. Phenylaminotrinitrodimethylbenzimidazolone must therefore be assigned the structure of (XIII).

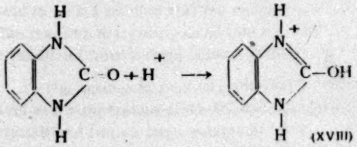
In the light of the foregoing considerations we can confidently assert that the di-(phenylamino)-dinitro derivatives from 4,5,6,7-tetranitrobenzimidazolone and from 4,5,6,7-tetranitro-1,3-dimethylbenzimidazolone (XI) have the structures of (XV) and (XVII) respectively, and not the structure of 5,6-di-(phenylamino)-4,7-dinitro derivatives, for if the contrary had been the case it would have been difficult to account for the difference in behavior of 4,5,6,7-tetranitrobenzimidazolone (VI) and 4,5,6,7-tetranitro-1,3-dimethylbenzimidazolone (XI) when treated with aniline in water in the cold.

The above-described products of nitration of benzimidazolone and of its 1,3-dimethyl analog and their interrelation are represented in the scheme.

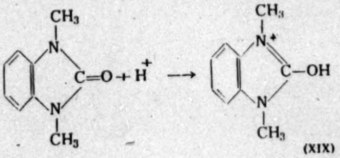
The facts presented, which show that benzimidazolone and its 1,3-dimethyl analog behave in exactly the same manner during nitration, enable us to refute the statement of Kym and Ratner [1] to the effect that benzimidazolone is in the tautomeric form of 2-hydroxybenzimidazole during this reaction.

On the other hand, our observation of the similarity in the direction of nitration of derivatives of benzimidazole and of the two products investigated (with a different structure of the heterocycle) can only be explained on the assumption that the latter add on a proton to the oxygen (like urea in a strongly acid medium) and enter into the nitration reaction in the form of the cations (XVIII) and (XIX) which do not differ from the cations of other derivatives of benzimidazole.

The exceptional ease of entry of four nitro groups with formation of the tetranitro derivatives (VI) and (XI) can be accounted for by the strongly activating influence on the benzene ring of benzimidazolone and 1,3-dimethylbenzimidazolone of the hydroxy groups in the 2-position of cations (XVIII) and (XIX).

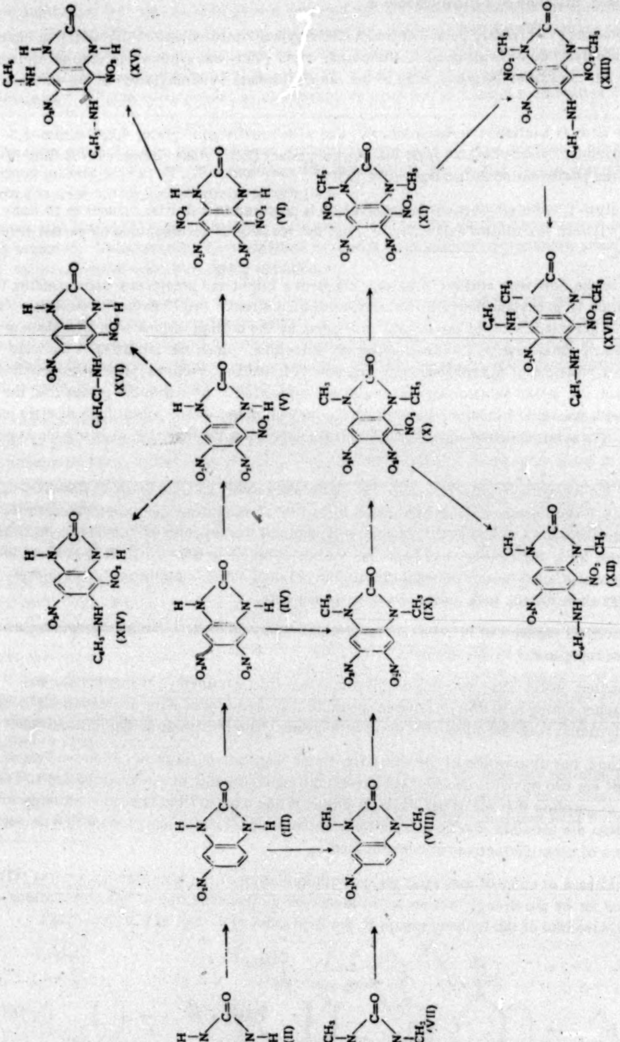


(XVIII)



(XIX)

SCHEME


(II)
(III)
(IV)
(V)
(VI)
(VII)
(VIII)
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(XI)
(XII)
(XIII)
(XIV)
(XV)
(XVI)
(XVII)
H–N
C=O
N–H
CH₃
O₂N
NO₂
C₆H₅–NH
C₆H₄Cl–NH
C₆H₅

EXPERIMENTAL

Nitration of benzimidazolone

5-Nitrobenzimidazolone. 10 g of benzimidazolone was dissolved in 45 ml concentrated sulfuric acid (d 1.84) in such a manner that the temperature did not rise above 10°. The solution was cooled to 0° and at this temperature and with vigorous stirring a nitrating mixture of 3.3 ml fuming nitric acid and 3.7 ml sulfuric acid (d 1.84) was added in the course of 2 hours. After stirring for a short period, the reaction mass was poured into water and the precipitate was filtered and washed with water until no longer acid to congo. The product was treated with 1 liter of boiling water and filtered hot. The residue on the filter was dissolved in boiling 60% alcohol from which, on cooling, 6.25 g of long yellow fibers came down. The product melted at 306° and did not give a depression of melting point in admixture with 5-nitrobenzimidazolone prepared from 1,2-diamino-4-nitrobenzene and urea [2].

Another 3.1 g of 5-nitrobenzimidazolone was isolated after prolonged purification of the precipitates from the aqueous extract and of the concentrated alcoholic mother liquor. Yield 68.5% calculated on the pure product.

4-Nitrobenzimidazolone. 0.25 g 1,2-diamino-3-nitrobenzene, prepared by Borsche's method [5] from 2,6-dinitroaniline, was thoroughly mixed with 0.5 g urea in a porcelain crucible, and the mixture was slowly heated on an oil bath. The mixture fused at 140° and the melt solidified at 190° after holding at that temperature for a short time. The mass was then cooled and dissolved with gentle heating in 7% caustic alkali; the solution was filtered and the mother liquor was neutralized with hydrochloric acid. The precipitate was washed with water and dried, and then recrystallized from a large volume of alcohol. 4-Nitrobenzimidazolone is obtained in the form of light-greenish flakes which decompose at 342° without melting.

Found %: N 23.35, 23.03. $C_7H_5O_3N_3$. Calculated %: M 23.46.

5,6-Dinitrobenzimidazolone. a) From benzimidazolone. 2 g benzimidazolone was dissolved in 13 ml H_2SO_4 (d 1.84) at 5-10° and to the stirred solution was added a nitrating mixture of 2 ml fuming nitric acid and 7 ml sulfuric acid (d 1.84) in such a manner that the temperature of the reaction mass did not rise above 0°. After an hour's stirring, the reaction mass was poured into ice and the precipitate was recrystallized from a large volume of water or reprecipitated from dilute caustic alkali solution with hydrochloric acid. Yield 94% reckoned on the crude product. The product was identical with that obtained by nitration of 5-nitrobenzimidazolone to the dinitro derivative.

b) From 5-nitrobenzimidazolone. 2 g 5-nitrobenzimidazolone was dissolved in 15 ml sulfuric acid (d 1.84) in such a manner that the temperature did not rise above 10°. The solution was cooled to 0° and dropwise addition was made, with vigorous stirring, of a nitrating mixture comprising 0.75 ml fuming nitric acid and 10 ml sulfuric acid (d 1.84). The reaction mass was stirred one hour at 0° and poured into ice. The precipitate was collected and washed with water. Recrystallization from a large volume of water gave long needles which did not melt at 315°. Yield 74% reckoned on the pure product.

Found %: C 37.69; H 2.08. $C_7H_4O_5N_4$. Calculated %: C 37.51; H 1.80.

4,5,6-Trinitrobenzimidazolone. To 2 g benzimidazolone, dissolved in 13 ml sulfuric acid (d 1.84), was added dropwise, with stirring, a nitrating mixture of 2 ml fuming nitric acid and 7 ml sulfuric acid in such a manner that the temperature did not rise above 40°; it was then held for a short period at 45°. The reaction mass was poured into ice, and the precipitate was filtered, washed with water and recrystallized from a large volume of water. Yield 75% reckoned on the pure product.

The same substance was obtained by adding 3 g of 5-nitrobenzimidazolone to 24 ml fuming nitric acid at a temperature of 40-45° and then pouring the reaction mass into ice. The precipitate was recrystallized from a large volume of water. Yield 55% reckoned on the pure product. It was identical with the product obtained from 5,6-dinitrobenzimidazolone. 4,5,6-Trinitrobenzimidazolone forms small needles, melting unsharply at 258°.

Found %: C 31.55; H 1.77; N 26.32, 25.83. $C_7H_3O_7N_5$. Calculated %: C 31.24; H 1.12; N 26.02.

Trinitrobenzimidazolone readily forms a phenylaminodinitro derivative when shaken in the cold with an aqueous emulsion of aniline. 0.25 g of trinitrobenzimidazolone was stirred in the cold for half an hour with 25 ml of 10% aniline in water. The reaction mass was then acidified with hydrochloric acid to remove the excess of aniline. After filtration and washing, the precipitate was dried and recrystallized from glacial acetic acid and then from ethyl acetate. 5-(Phenylamino)-4,6-dinitrobenzimidazolone forms fine, red needles melting at 284°.

Found %: N 22.31, 22.28. $C_{13}H_9O_5N_5$. Calculated %: 22.22.

5-(p-Chlorophenylamino)-4,6-dinitrobenzimidazolone was prepared by mixing 0.6 g p-chloroaniline (in 8 ml alcohol) with a solution of 1.1 g 4,5,6-trinitrobenzimidazolone in 15 ml alcohol and 40 ml acetone. The mixture was kept in the cold for 2 days, evaporated on a water bath to 1/4 of its volume and cooled. The precipitate was recrystallized from alcohol. M. p. 309° (decomp.). Microscopic dark-red needles. Yield 0.4 g of analytically pure substance.

Found %: C 44.91; H 2.50. $C_{13}H_8O_5N_5Cl$. Calculated %: C 44.65; H 2.30.

4,5,6,7-Tetranitrobenzimidazolone. 4.15 g of benzimidazolone was dissolved in 30 ml concentrated sulfuric acid and addition was made to the reaction mass at 30-40° of 6 ml fuming nitric acid mixed with 19 ml concentrated sulfuric acid. The reaction mass was then poured into ice. The precipitate was washed with water until neutral to congo and dried. Weight of precipitate 7 g. The dry precipitate was then put into a mixture of 24 ml fuming nitric acid (d 1.5) and 59 ml monohydrate and the mixture was heated on a boiling water bath for 30 minutes and then poured into ice. Weight of precipitate 5 g. After recrystallization from chlorobenzene containing acetone, the compound had the form of stout, large needles containing chlorobenzene and losing it after drying for 4 days at 100°. M. p. 311° (decomp.).

Found %: C 27.05; H 0.93; N 26.70, 26. 48. $C_7H_2O_9N_6$. Calculated %: C 26.75; H 0.64; N 26.76.

Tetranitrobenzimidazolone is converted into the di-(phenylamino)- derivative when shaken in the cold with aniline in water.

4,6-Di-(phenylamino)-5,7-dinitrobenzimidazolone is obtained as dark-red microscopic crystals when recrystallized from glacial acetic acid. The crystals are easily electrified. M. p. 287° with decomposition.

Found %: C 55.88; H 2.45; N 20.66, 20.71. $C_{19}H_{14}O_5N_6$. Calculated %: C 56.18; H 3.45; N 20.69.

Nitration of 1,3-dimethylbenzimidazolone

5-Nitro-1,3-dimethylbenzimidazolone was obtained both by nitration of 1,3-dimethylbenzimidazolone and by methylation of 5-nitrobenzimidazolone.

Nitration was performed under the same conditions as the nitration of benzimidazolone to the mononitro derivative. The crude product was recrystallized from a large volume of water and then from a very much smaller volume of alcohol. The precipitate formed after cooling was contaminated with dinitro product. After slight concentration of the alcoholic mother liquor, slightly greenish, beautiful needles of 5-nitro-1,3-dimethylbenzimidazolone came down. M. p. 204-205°. Yield 60%.

24 g of 5-nitrobenzimidazolone was dissolved by heating in 300 ml sodium hydroxide. Dropwise addition was then made at 80° and with good stirring of 28 ml dimethyl sulfate. The precipitate partly dissolved when 35 ml of 35% sodium hydroxide was added to the reaction mass and appreciably increased in size when dropwise addition was made of 28 ml dimethyl sulfate. The temperature of the reaction mass was raised to 90° by external heating, 10 ml of 35% sodium hydroxide was added, and the stirred reaction mass was heated for an hour. The precipitate was filtered, washed with water until free from alkali, and recrystallized from alcohol. Yield 65% reckoned on the pure product. The compound melts at 205-206°

and does not give a depression of melting point in a mixed test with the product of direct mononitration of 1,3-dimethylbenzimidazolone.

Found %: C 52.25; H 4.68, N 20.28, 20.53. $C_9H_9O_3N_3$. Calculated %: C 52.17; H 4.38; N 20.28.

5,6-Dinitro-1,3-dimethylbenzimidazolone. a) From 5-nitro-1,3-dimethylbenzimidazolone. 1.85 g of 5-nitro-1,3-dimethylbenzimidazolone was dissolved in conc. sulfuric acid (d 1.84) at a temperature below 10° and to the solution was added a mixture of 0.6 ml fuming nitric acid and 5 ml sulfuric acid (d 1.84) at below 0°. After one hour's stirring, the reaction mass was poured into ice and the precipitate was recrystallized from aqueous acetic acid. The stout, red needles of 5,6-dinitro-1,3-dimethylbenzimidazolone melt at 295°.

b) From 5,6-dinitrobenzimidazolone. 2 g 5,6-dinitrobenzimidazolone was dissolved with gentle heating in 20 ml of 4% caustic alkali, and dropwise addition of 2 ml dimethyl sulfate was made at 60-65° followed by 16 ml 5% alkali. The solution was heated to 90° and a further 2 ml dimethyl sulfate and 16 ml alkali was added. The reaction mass was stirred at the boil for 1 hour and 10 ml 5% alkali was added. After cooling, the precipitate was filtered, washed with water until free from alkali and recrystallized from acetic acid. Yield 70% reckoned on the pure substance. The product melts at 295° and does not give a depression of melting point in admixture with the product of direct mononitration of 5-nitro-1,3-dimethylbenzimidazolone.

Found %: N 22.46, 22.38. $C_9H_8O_5N_4$. Calculated %: N 22.22.

4,5,6-Trinitro-1,3-dimethylbenzimidazolone. a) 1 g of 5,6-dinitro-1,3-dimethylbenzimidazolone was added at 35-45° to 10 ml fuming nitric acid. The reaction mass was then poured into ice and the precipitate was collected and washed with water. Recrystallization from 110 ml 50% acetic acid gave 0.7 (63.5%) of thin plates with m.p. 207°.

b) The same product was also obtained by dinitrating 5-nitro-1,3-dimethylbenzimidazolone. 0.5 g of the latter was added to 6 ml fuming nitric acid and the reaction mass was later poured into water. The precipitate was recrystallized from aqueous acetic acid. Yield 53%.

Found %: C 36.29, 36.38; H 2.52, 2.39; N 23.55, 23.60. $C_9H_7O_7N_5$. Calculated %: C 36.37; H 2.37; N 23.57.

Preparation of 5-(phenylamino)-4,6-dinitro-1,3-dimethylbenzimidazolone from 4,5, 6-trinitro-1,3-dimethylbenzimidazolone was effected by a method similar to that used for the preparation of 5-(phenylamino)-4,6-dinitrobenzimidazolone. The yield of crude product was approximately quantitative. The compound forms bright-red needles, crystallizing from glacial acetic acid. M. p. 204°.

Found %: N 20.22, 20.45. $C_{15}H_{13}O_5N_5$. Calculated %: N 20.41.

4,5,6,7-Tetranitro-1,3-dimethylbenzimidazolone. 5 g of 1,3-dimethylbenzimidazolone was added in small portions to 30 ml monohydrate at 40° and to the reaction mass was added 6 ml fuming nitric acid dissolved in 10 ml sulfuric acid (d 1.84). The mass was run into ice and the precipitate was collected, washed with water, dried and put into a mixture of 15 ml fuming nitric acid and 45 ml monohydrate. The mass was heated 15 minutes on a boiling water bath;* a crystalline product floated to the surface and was filtered on a glass filter.** The precipitate was washed on the filter with a mixture of 5 ml fuming nitric acid and 5 ml monohydrate, then with 2 ml glacial acetic acid and a large amount of water. Recrystallization from glacial acetic acid gave very thin rhombic plates of analytically pure 4,5,6,7-tetranitro-1,3-dimethylbenzimidazolone, decomposing at about 290° with copious evolution of gas, Yield 53%.

Found %: C 32.03; H 1.80, N 24.43. $C_9H_6O_9N_6$. Calculated: C 31.59; H 1.77; N 24.56.

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* If heated for a longer period the precipitate gradually dissolves and gas is evolved.

** When the mother liquor is poured into ice, a precipitate is formed which after recrystallization from acetic acid consists of a mixture of products of oxidation of the methyl groups of tetranitrodimethylbenzimidazole.

Treatment of 1.2 g 4,5,6,7-tetranitro-1,3-dimethylbenzimidazolone with aniline in water (5 ml aniline in 50 ml water) in the cold led to instantaneous formation of a red substance which dissolved completely in the excess of aniline. After 30 minutes stirring, the reaction mass was slowly acidified with hydrochloric acid (10 ml d 1.19) and the precipitate was filtered, washed with water, dried from glacial acetic acid and treated with chloroform. The $CHCl_3$ solution was filtered and diluted with glacial acetic acid. 5-(Phenylamino)-4,6,7-trinitro-1,3-dimethylbenzimidazole came down on standing. Microscopic, bright-red needles with m. p. 175-176°.

Found %: C 46.24; H 3.02; N 21.73, 21.62. $C_{15}H_{12}O_7N_6$. Calculated %: C 46.41; H 3.11; N 21.65.

A mixture of the above-described compound and 4,5,6,7-tetranitro-1,3-dimethylbenzimidazolone was subsequently separated from the mother liquors after purification of the former. This mixture was treated for 1 hour with boiling 10% aniline-in-water (25 ml). The precipitate formed after acidification was recrystallized from glacial acetic acid and then from a mixture of ethyl acetate and benzene. The resultant light-red, easily electrified microscopic crystals with m. p. 251° correspond in structure to 5,7-di-(phenylamino)- 4,6-dinitro-1,3-dimethylbenzimidazolone.

Found %: C 58.37; H 3.38; N 19.58; 19.37. $C_{21}H_{18}O_5N_6$. Calculated %: C 58.06; H 4.18; N 19.35.

SUMMARY

1. Benzimidazolone and 1,3-dimethylbenzimidazolone undergo nitration with remarkable facility with formation successively of the 5-nitro derivative, the 5,6-dinitro derivative, the 4,5,6-trinitro derivative and, as the product of exhaustive nitration, the vicinal tetranitro derivative.

2. The trinitro and tetranitro derivatives of benzimidazolone and 1,3-dimethylbenzimidazolone undergo replacement of their labile nitro groups by aniline in the cold.

3. The similarity in the direction of nitration of benzimidazolone and 1,3-dimethylbenzimidazolone on the one hand and that of other benzimidazole derivatives on the other hand confirms the previously enunciated [4] hypothesis of the formation by benzimidazolone and its analogs of cations in a strongly acid medium, due to the addition of a proton from the medium to an oxygen atom. The results also reveal the untenability of the claim that benzimidazolone functions in this reaction in the tautomeric form of 2-hydroxybenzimidazole.

LITERATURE CITED

[1] L. S. Efros, J. Gen. Chem. 22, 1008 (1952); (T. p. 1063);* Bamberger and Berle, Ann. 273, 340, (890).

[2] O. Kym amd L. Ratner, Ber. 45, 3238 (1912).

[3] G. T. James and E. E. Turner, J. Chem. Soc. 1950, 1515.

[4] L. S. Efros, B. A. Porai-Koshits and S. G. Farbenshtein, J. Gen. Chem. 23, 1691 (1953). (T. p. 1779).*

[5] Borsche, Ann. 379, 163 (1911).

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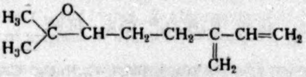
* T. p. = C. B. Translation pagination.

INVESTIGATION OF MYRCENE DIOXIDE

G. V. Pigulevsky and N. A. Adrova

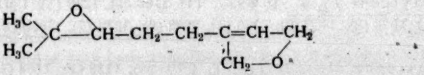
In a communication [1] on the preparation of myrcene monoxide we assigned the structure of 2,3-oxido-2-methyl-6-methylene-octene-7 to this substance.



Myrcene dioxide is a co-product of the preparation of the monoxide by the oxidation of myrcene with acetyl hydroperoxide. Formation of the dioxide goes at the expense of partial polymerization of myrcene and release of an excess of active oxygen.

The objective of the present work was the elucidation of the structure of myrcene dioxide and the study of some of its properties.

We resorted to optical methods for elucidation of the structure of myrcene dioxide since it is hardly possible to obtain unambiguous results by chemical methods. One oxide ring in myrcene dioxide is undoubtedly in the same position as in myrcene monoxide. The position of the second ring remains uncertain. Three variants are possible: an oxide ring is formed by carbon atoms 8 and 6' of (I), an oxide ring is formed with participation of carbon atoms 7 and 8 of (II), and an oxygen atom is linked to carbon atoms 6 and 6' of (III).



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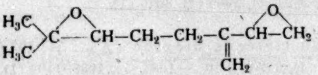

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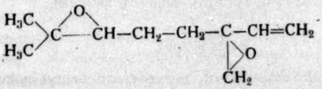
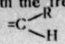


(III)

We plotted the Raman spectrum. The spectrum of myrcene dioxide contains a line with the frequency $\Delta\nu 1639$ cm^{-1}, which is characteristic of a primary-secondary double bond [2]. A primary-secondary bond is present in formula (III). In the case of a secondary-tertiary or primary-tertiary bond (I or II) the spectrum should contain lines with the frequencies $\Delta\nu 1675$ cm^{-1} and 1653 cm^{-1}, but such lines are absent from the spectrum plotted.

We therefore arrived at the conclusion that the structure of 2,3,6,6'-di-oxido-2 methyl-6-methylene-octene-7 (III) must be assigned to myrcene dioxide. This formula is also consistent with the presence in the spectrum of a line with the frequency $\Delta\nu$ 3010 cm^{-1}, which is characteristic of the deformation vibration δ (CH) inherent in the  $=C\langle^{R}_{H}$ group.

Myrcene dioxide was subjected to hydrogenation in presence of platinum black. The Raman spectrum is deficient in lines with frequencies characteristic of double bonds. The line with the frequency $\Delta\nu$ 3010 cm^{-1} also disappeared.

Dihydromyrcene dioxide must accordingly possess the structure of 2,3,6,6'-dioxido-2-methyl-6-methylene-octane.

EXPERIMENTAL

Myrcene. Linalool from coriander oil was subjected to dehydration over iodine at reduced pressure (150-160 mm) as described by B. A. Arbuzov [3].

Constants of myrcene: b. p. 57° (13 mm), d_4^{20} 0.8077, n_D^{20} 1.4737, MR_D 47.71; calc. 46.97.

The Raman spectrum indicates the presence of the β-form.

Myrcene dioxide. Oxidation of myrcene (0.81 mole) with acetyl hydro-peroxide (0.94 mole) in ether solution gave, apart from myrcene monoxide (73-75° at 14 mm), a fraction with b.p. 104-106° (18 mm).

d_4^{20} 0.9438, n_D^{20} 1.45145, MR_D 48.02. $C_{10}H_{16}O_2F$ Calc. 46.80.

Found %: C 71.11, 71.20; H 9.83, 9.76. M 164.9, 164.7 $C_{10}H_{16}O_2$. Calculated %: C 71.34; H 9.49. M 168.

Catalytic hydrogenation of myrcene dioxide. 20 g myrcene dioxide was taken with 2 g platinum oxide. Total volume of hydrogen taken up was 2630 ml (0° and 760 mm); calculated volume 2666 ml. The product of hydrogenation was distilled to give a fraction with b. p. 79-81° (12 mm):

d_4^{20} 0.8956, n_D^{20} 1.4175, MR_D 47.78. $C_{10}H_{18}O_2$. Calc. 47.24.

Found %: C 70.15, 70.38; H 10.73, 10.88. $C_{10}H_{18}O_2$. Calculated %: C 70.59; H 10.59.

Raman spectra. The spectra were obtained with the help of an ISP-51 three-prism spectrograph. Exposure for 4 and 6 hours with a slit width of 0.01 mm.

Spectrum of myrcene ($\Delta\nu$): 896 (1), 1166 (1), 1239 (1), 1291 (3), 1321 (1), 1370 (1), 1420–1457 (1), 1633 (10), 1676 (2), 2862 (0), 2926 (1), 2973 (0), 3014 (1), 3059 (0), 3100 (0).

Spectrum of myrcene dioxide ($\Delta\nu$): 679 (4), 1118 (1), 1164 (1), 1285 (2), 1322 (3), 1380 (2), 1417 (4), 1465 (1), 1639 (10), 2923 (2), 2963 (1), 3010 (1).

Spectrum of hydrogenated myrcene dioxide ($\Delta\nu$): 197 (1), 615 (1), 636 (1), 680 (2), 745 (1), 797 (2) – 826 (1), 869 (1), 972 (1), 1035– 1061 (1), 1088–1104 (1), 1144 (1)– 1164 (0), 1207 (1), 1287 (1), 1345 (1), 1383 (1), 1432 (3), 1467 (3), 2928 (4), 2972 (2).

SUMMARY

Myrcene dioxide, formed during the oxidation of myrcene with acetyl hydroperoxide, can be assigned the structure of 2,3,6,6'-dioxide-2-methyl-6-methylene-octene-7 (III).

Dihydromyrcene dioxide is formed on hydrogenation of myrcene dioxide.

LITERATURE CITED

[1] G. V. Pigulevsky and N. A. Prokudina, Proc. Acad. Sci. USSR 67, 511 (1949).

[2] G. V. Pigulevsky and A. T. Ryskalchuk, Trans. BIN, Acad. Sci. USSR, Series V, No. 5, 149 (1955).

[3] B. Arbusoff and W. Abramoff, Ber, 67, 1943 (1934).

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2-PROPYLCAMPHANE AND ITS DERIVATIVES

A. S. Zabrodina, K. M. Suvorova and S. Z. Sheinina

Camphane and its derivatives have been the subject of numerous investigations for a long time, whereas relatively little attention has been paid to homologs of camphane.

2-Allylcamphane (I) can be used for the synthesis of homologs of camphane with substituents in the 2-position and having the composition C_{13} and higher. 2-Allylcamphane is obtained by the action of allyl bromide on the product of reaction of magnesium with bornyl chloride [1, 2].

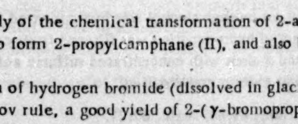
It was established [2] that the action of magnesium on bornyl chloride (trans) gives a mixture of approximately equal amounts of bornyl magnesium chloride (trans), isobornyl magnesium chloride (cis) and bornyl-isobornyl-magnesium, due to which a mixture of cis- and trans-isomers ought to be obtained by subsequent treatment with reactants. It was also shown [1, 3] that the speed of reaction of both carbon dioxide and allyl bromide with bornyl magnesium chloride is higher than with isobornyl magnesium chloride, so that with an insufficient amount of carbon dioxide a mixture of acids with a predominant content of trans-isomer is obtained, i. e., bornyl carboxylic acid, while the action of an insufficient amount of allyl bromide on the Grignard compound gives trans-2-allylcamphane which Riviere [2] accordingly called "allyl-bornyl" [ ].

Riviere's allylbornyl was evidently not isolated in the pure state since it had a 3-degree boiling range and and no analysis was reported.

In a study of the chemical transformation of 2-allylcamphane we established that it adds on hydrogen with facility to form 2-propylcamphane (II), and also bromine to give 2-(β, γ-dibromopropyl)-camphane (III).

Addition of hydrogen bromide (dissolved in glacial acetic acid) to 2-allylcamphane does not follow the Markovnikov rule, a good yield of 2-(γ-bromopropyl)-camphane (VI) being obtained. Addition of hydrogen bromide in an aqueous medium to 2-allylcamphane is likewise mainly contrary to the Markovnikov rule although the yield is very much poorer. The structure of 2-(γ-bromopropyl)-camphane was verified by heating it with sodium acetate in glacial acetic acid to form 2-(γ-acetoxypropyl)-camphane (V) in good yield, and by saponification of the latter to form 2- (γ- hydroxypropyl)-camphane (VI). Determination of the content of primary alcohols by the method of Radcliffe and Chadderton [4] showed that the alcohol obtained is primary. Oxidation of 2- (γ-hydroxypropyl)-camphane both with potassium permanganate and with potassium dichromate gave camphane-2-propionic acid (VII), which affords further confirmation of the structure of the alcohol prepared. The main product of oxidation of 2-(γ-hydroxypropyl)-camphane with potassium dichromate was the camphane-2-propionate of 2-(γ -hydroxypropyl)-camphane (VIII).

We deviated from Riviere's procedure in taking an excess of allyl bromide for the preparation of 2-allylcamphane. Since, however, the yield of hydrocarbon did not exceed 30% and since, as was established [2], allyl bromide reacts selectively with bornyl magnesium chloride to give mainly a trans-isomer, we suggest that 2-allylcamphane and all the compounds that we prepared from it are predominantly trans-isomers.



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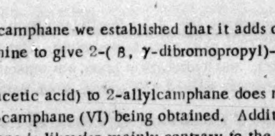

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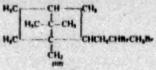
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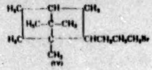
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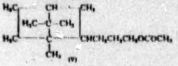
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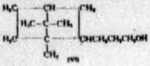
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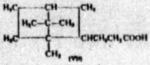
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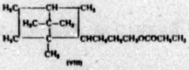
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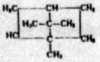

EXPERIMENTAL

2-Allylcamphane (I). 4 g ethyl bromide in 8 ml absolute ether was added to 15 g magnesium. After the reaction had commenced, a solution of 100 g bornyl chloride in 150 ml absolute ether was gradually added dropwise with constant stirring, after which the mixture was heated for 2 hours on a water bath. To the reaction mixture was then slowly added (dropwise) a solution of 110 g allyl bromide in 110 ml absolute ether while cooling with ice. The mixture was allowed to stand overnight. Decomposition was effected with dilute ammonium chloride solution with addition of ice. The reaction product was extracted with ether. After removal of the ether the residue was distilled with steam to separate it from the difficultly volatile dibornyl. The product was dried with calcium chloride, boiled for 2 hours over sodium and fractionated. Yield 37 g 2-allylcamphane.

B. p. 216.5 – 217° (753.5 mm), 81–81.5° (9 mm), d_4^{20} 0.8753, n_D^{20} 1.4759; MR_D 57.44; Calc. 57.37.

Found %: C 87.66; H 12.34. $C_{13}H_{22}$. Calculated %: C 87.56; H 12.44.

Literature data for "allylbornyl" (2-allylcamphane) [2]: B. p. 89–92° (15 mm), d_{18}^{18} 0.898, n_D^{18} 1.4815.

2-Propylcamphane (II). 5.3 g 2-allylcamphane in 10 ml methyl alcohol was hydrogenated in presence of platinum black (0.1 g) at room temperature. The product of hydrogenation was filtered from catalyst and diluted with water; the hydrocarbon layer was separated and shaken with concentrated sulfuric acid. The 2-propylcamphane was washed with water, dried, boiled over sodium and distilled.

B.p. 219–219.5° (753.5 mm), d_4^{20} 0.8639, n_D^{20} 1.4659; MR_D 57.83; calc. 57.77.

Found %: C 86.42, 86.53; H 13.35, 13.25. $C_{13}H_{24}$. Calculated %: 86.58; H 13.42.

2-(β, γ-Dibromopropyl)-camphane (III). To 5 g 2-allylcamphane, dissolved in 15 ml chloroform, was added a solution of 4.6 g bromine in 7 ml chloroform while cooling with ice. The reaction liquid was washed with sodium carbonate solution and dried. The chloroform was driven off and the residue distilled in vacuum to give 7 g 2-(β, γ-dibromopropyl)-camphane.

B. p. 134.5– 135° (3.5 mm); d_4^{20} 1.4213, n_D^{20} 1.5310. MR_D 73.62, calc. 73.36.

Found %: C 46.39, 46.34; H 6.55, 6.56; Br 47.10, 47.26. $C_{13}H_{22}Br_2$. Calculated %: C 46.17; H 6.55; Br 47.27.

2-(γ -Bromopropyl)-camphane (IV). 27.5 g 2-allylcamphane was shaken with 57 ml saturated solution of hydrogen bromide in glacial acetic acid for 30 hours. The reaction product was poured into water, the resultant oil was separated, diluted with ether, washed with sodium bicarbonate solution and then with water, and dried. Distillation gave 35.5 g 2- (γ -bromopropyl)-camphane.

B. P. 122-123° (3.5 mm), d_4^{20} 1.1698, n_D^{20} 1.5023, MR_D 65.44; Calc. 65.60.

Found %: C 60.47, 60.31; H 8.78, 8.81; Br 30.83, 30.79. $C_{13}H_{23}Br$. Calculated %: C 60.23; H 8.93; Br. 30.83.

2- (γ - Acetoxypropyl) - camphane (V). 15 g 2-(γ-bromopropyl)-camphane was introduced dropwise with stirring and heating to 150-153° into 16 g of fused sodium acetate in 20 ml glacial acetic acid. Heating and stirring were continued for 12 hours. Into the cooled reaction mixture was run 100 ml water; the resultant oil was extracted with ether, washed and dried. Removal of the ether and distillation of the residue gave 11.5 g 2-(γ-acetoxypropyl)-camphane.

B. P. 115-116° (2.5 mm), d_4^{20} 0.9667, n_D^{20} 1.4700, MR_D 68.79; Calc. 68.72.

Found %: C 75.43, 75.64; H 11.09, 11.08. $C_{15}H_{26}O_2$. Calculated %: C 75.58; H 10.99.

2-(γ- Hydroxypropyl)-camphane (VI). 11.3 g 2-(γ-acetoxypropyl)-camphane was heated on a water bath for 6 hours with alcoholic alkali (6 g KOH in 35 ml ethyl alcohol), after which the main bulk of ethyl alcohol was distilled off; the residue was diluted with water, extracted with ether and dried with potassium carbonate. Removal of the ether and distillation in vacuum gave 7.5 g 2-(γ-hydroxypropyl)-camphane.

B. p. 133.5– 135° (4mm), d_4^{20} 0.9518, n_D^{20} 1.4863, MR_D 59.25. Calc. 59.19.

Found %: C 79.28, 79.38; H 12.49, 12.44. $C_{13}H_{24}O$. Calculated %: C 79.53; H 12.32.

Primary alcohols were determined by the method of Radcliffe and Chadderton [4] which is based on the quantitative conversion of primary alcohols into acid phthalic esters when treated with phthalic anhydride in pyridine solution. The determination showed that the prepared 2-(γ-hydroxypropyl)-camphane contained up to 97.18 % primary alcohols. (Accuracy of method 2-3%.)

The phenylurethane of 2-(γ-hydroxypropyl)-camphane had m. p. 80.5-81.2° after recrystallization from alcohol.

Found %: C 76.26; H 9.31. $C_{20}H_{29}O_2N$. Calculated %: C 76.15; H 9.27.

Acid phthalic ester of 2-(γ-hydroxypropyl)-camphane was prepared from a pyridine solution of its potassium salt which was formed during quantitative determination of 2-(γ-hydroxypropyl)-camphane. After evaporation of the solution to dryness in vacuum, the potassium salt of the acid phthalic ester was extracted with ether; the ether was driven off and the residue dissolved in water and acidified. The precipitated acid phthalic ester was recrystallized from dilute ethyl alcohol; m.p. 140.5-141.5°.

Found %: C 73.31, 73.36; H 8.25, 8.22. $C_{21}H_{28}O_4$. Calculated %: C 73.23; H 8.19.

Oxidation of 2-(γ-hydroxypropyl)-camphane with potassium permanganate. 1 g of 2-(γ-hydroxypropyl)-camphane was shaken at room temperature for 50 hours with an alkaline solution of potassium permanganate (0.7 g $KMnO_4$ and 0.1 g KOH in 20 ml water) until the solution was decolorized. The manganese dioxide was filtered off and washed with hot water. The solution was evaporated and acidified with sulfuric acid. The precipitated camphane-2-propionic acid (VII) was recrystallized from dilute ethyl alcohol; m. p. 89.5-90.5°.

Found %: C 74.44, 74.41; H 10.60, 10.54. $C_{13}H_{22}O$. Calculated %: C 74.24; H 10.54.

Oxidation of 2-(γ-hydroxypropyl)-camphanewith potassium dichromate. A solution of 3 g potassium dichromate and 4 ml sulfuric acid in 15 ml water was added dropwise to 6 g 2-(γ-hydroxypropyl)-camphane in 15 ml water. The reaction product was distilled with steam; a small amount of oil came over which gave a violet color with fuchsinesulfurous acid, indicating the presence of an aldehyde. The substance remaining in the distillation flask was extracted with ether. The ether extract was washed with 10 % sodium hydroxide solution to remove acids, then with water, and dried with sodium sulfate. The ether was driven off and the residue distilled in vacuum to give 2.5 g camphane-2-propionate of 2-(γ-hydroxypropyl)-camphane (VIII).

B. p. 198-202° (6 mm), d_4^{20} 0.9616, n_D^{20} 1.4900, MR_D 116.0. Calc. 115.1.

Found %: C 80.17; H 11.50. $C_{26}H_{44}O_2$. Calculated %: C 80.35; H 11.41.

The alkaline solution, obtained as described above, was evaporated to a small volume and then acidified. Yield 0.34 g camphane-2-propionic acid with m. p. 89.5-90.5° (from dilute alcohol).

1.2 g camphane-2-propionate of 2-(γ-hydroxypropyl)-camphane was hydrolyzed with alcoholic potash (0.5 g KOH in 2 ml ethyl alcohol). The reaction mass was diluted with water and extracted with ether; the aqueous solution was evaporated and acidified to give 0.25 g camphane-2-propionic acid with m. p. 89-90° (from dilute alcohol).

SUMMARY

1. A new homolog of camphane—2-propylcamphane—and the following derivatives were prepared: 2-(β, γ-dibromopropyl)-camphane, 2-(γ-bromopropyl)-camphane, 2-(γ-acetoxypropyl)-camphane, 2-(γ-hydroxypropyl-camphane, camphane-2-propionic acid, and the camphane-2-propionate of 2-(γ-hydroxypropyl)-camphane.

2. Addition of hydrogen bromide to allylcamphane proceeds contrary to the Markovnikov rule with formation of 2-(γ-bromopropyl)-camphane.

LITERATURE CITED

[1] G. Vavon, C. Riviere, Compt. rend. 213, 1016 (1941.).

[2] C. Riviere, Ann. Chim. (12) 1, 157 (1946).

[3] M. deBotton, Bull. Soc. Chim. 1955, 816.

[4] L. G. Radcliffe and E. Chadderton, Perfume Record, 17. 352 (1926).

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Moscow State University

PREPARATION OF QUATERNARY SALTS OF WEAK ORGANIC BASES

A. I. Kiprianov and A. I. Tolmachev

Quaternary salts of heterocyclic bases are intermediates for the synthesis of cyanine dyes and many pharmaceutical preparations.

Little attention has hitherto been paid to the clarification of the relation between the structure of alkylating agents and their activity. N. A. Menshutkin [1] and later a series of other authors investigated the speed of formation of quaternary salts during the action of alkyl halides on tertiary amines in relation to the structure of the alkyl, the nature of the halogen and the character of the solvent. Alkyl halides are relatively weak alkylating agents. Dimethyl sulfate [2] has found wide application for alkylations since the start of the present century. Dimethyl sulfate and diethyl sulfate are considerably more active than alkyl halides. They form quaternary salts with bases with which alkyl iodides do not react, but their field of application is limited mainly to the introduction of methyl and ethyl groups. Higher dialkyl sulfates are not readily accessible and have low reactivity.

The work of V. M. Rodionov [3] brought esters of p-toluenesulfonic acid and of benzenesulfonic acid into use. Although they are less active than dimethyl sulfate, they facilitate the introduction of higher alkyls; moreover, unlike dimethyl sulfate, these esters have low toxicity. The range of alkylating agents now applicable to the preparation of quaternary salts is limited to the compounds mentioned above. Many weak or unstable bases are known which cannot be converted into quaternary salts by any of these alkylating agents.

We have undertaken a search for stronger alkylating agents, starting from the consideration that the ability of an alkyl ester of an acid to donate an alkyl to a base is in direct relationship to the strength of the acid, i. e., to its ability to donate a proton to the base. The stronger the acid the stronger is the alkylating ability of its ester. The most active preparations must be esters of perchloric acid but they are not applicable in practice due to their instability. Esters of benzenesulfonic acid have medium activity but their alkylating power can be considerably intensified by the introduction of negative substituents into the benzene ring, for example nitro groups which repel electrons and increase the strength of the acid.

In a series of studies it was shown that esters of benzenesulfonic acids containing negative substituents in the benzene ring are stronger electrophilic agents. As far back as 1895 Kastle and Murrill [4], and then in 1910 Boyle [5], observed that the introduction of a halogen atom into the benzene ring of the ethyl ester of benzenesulfonic acid increases its ability to ethylate alcohols. In 1931 Demeny [6] showed that the nitro groups in the benzene ring of esters of benzenesulfonic acids accelerate their hydrolysis, while a methyl in the para-position retards hydrolysis. Other papers in more recent years have reported the acceleration of hydrolysis and alcoholysis of esters of benzenesulfonic acids under the influence of negative substituents [7].

Nobody has previously undertaken a comparison of the activity of esters of different benzenesulfonic acids in the formation of quaternary salts of organic bases. Esters of dinitrobenzenesulfonic acids have not even been generally prepared. We carried out a kinetic study to compare the speeds of formation of quaternary salts of one and the same base using already known alkylating agents as well as esters of nitrobenzenesulfonic acids.

The base selected was 2-methylbenzothiazole. The rate of formation of quaternary salts of 2-methylbenzothiazole was studied in toluene solution with methyl iodide, dimethyl sulfate and the methyl esters of twelve arylsulfonic acids: benzenesulfonic acid; p-toluenesulfonic acid; o-, m- and p-nitrobenzenesulfonic acids; 2,3-, 2,4-, 2,5-, 3,4- and 3,5-dinitrobenzenesulfonic acids; 2-nitro-4-chlorobenzenesulfonic acid and 2-nitro-4-trifluoromethylbenzenesulfonic acid. The reaction was carried out at temperatures of 70, 80, 90 and 100°. The reaction velocity was determined from the weight of quaternary salt separating from solution. The velocity constants, calculated from the equation for a bimolecular reaction, showed close similarity. The reaction of the methyl esters of 2,3-, 2,4- and 2,5-dinitrobenzenesulfonic acids and of 2-nitro-4-trifluoromethylbenzenesulfonic acid was studied at lower temperatures (30, 40, 50 and 60°) due to its high velocity, and the velocity constants at 80 and 90° were determined by extrapolation.

Results of measurements and calculations are set forth in Table 1.

TABLE 1

Alkylating agent	$K \cdot 10^5$ (liter/mole sec)				E(kcal)	$\log P_z$
	70°	80°	90°	100°		
CH_3I		0.48	0.92	1.70	16.6	5.0
p-$CH_3C_6H_4SO_3CH_3$		0.90	2.10	4.40	20.8	7.8
$C_6H_5SO_3CH_3$	1.0	2.2	4.6	9.4	19.2	7.2
p-$NO_2C_6H_4SO_3CH_3$	12.0	23.2	41.5		15.2	5.8
m-$NO_2C_6H_4SO_3CH_3$	16.7	33.4	61.3		16.6	6.8
$(CH_3)_2SO_4$	16.5	32.5	63.5		16.7	6.9
o-$NO_2C_6H_4SO_3CH_3$	109	207	371		15.7	7.0
3,4-$(NO_2)_2C_6H_3SO_3CH_3$ *	138	280	529		16.5	7.7
3,5-$(NO_2)_2C_6H_3SO_3CH_3$ *	167	300	562		15.0	6.8
2,4-$(NO_2)(Cl)C_6H_3SO_3CH_3$	198	377	645		14.6	6.6
2,4-$(NO_2)(CF_3)C_6H_3SO_3CH_3$ *		[920]	[1560]		13.4	6.3
2,5-$(NO_2)_2C_6H_3SO_3CH_3$ *		[1600]	[2670]		13.0	6.3
2,4-$(NO_2)_2C_6H_3SO_3CH_3$		[2040]	[3330]		12.5	6.0
2,3-$(NO_2)_2C_6H_3SO_3CH_3$ *		[2010]	[3500]		14.1	7.0

We see from the data of Table 1 that at 80° the methylating power of the methyl ester of m-nitrobenzenesulfonic acid is equal to that of dimethyl sulfate and 70 times greater than that of methyl iodide. The methyl ester of o-nitrobenzenesulfonic acid is approximately 6 times and the methyl esters of 2,3- and 2,4-dinitrobenzenesulfonic acids are 60 times more active than dimethyl sulfate — the strongest of the alkylating agents in use. The 2,5-dinitro ester approaches the 2,3- and 2,4-dinitro esters in methylating ability. The rise in the velocity of formation of quaternary salts in the case of nitro derivatives of benzenesulfonic acids is determined mainly by the fall in activation energy and sometimes also by the increase in magnitude of the exponent.

Of the three isomeric mononitrobenzenesulfonic acid methyl esters, the o-nitro ester gives the highest velocity constant; the m-nitro ester methylates 6 times more slowly, and the p-nitro ester 9 times more slowly. Hence the nitro group in the ortho position does not sterically hinder the methylation reaction. In the alkylation of amines with esters of sulfonic acids, the bond between the oxygen atom and the alkyl remote from the benzene ring is broken. Demeny [6], who studied the hydrolysis of ethyl esters of nitrobenzenesulfonic acids, also observed the highest rate of hydrolysis in the case of the ester of o-nitrobenzenesulfonic acid.

According to the data of N. A. Menshutkin [8] and more recent work [9], the velocity of formation of quaternary salts by the action of methyl iodide on tertiary amines increases very sharply on passing from less polar to more polar solvents. When using esters of benzenesulfonic acids, the polarity of the solvent has relatively little influence upon the reaction velocity. In Table 2 are given the velocity constants of the reaction of methyl esters of two arylsulfonic acids with 2-methylbenzothiazole in four solvents at 70°.

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* Esters of previously unknown sulfonic acids.

TABLE 2

Solvent	Dielectric constant at 20°	$K \cdot 10^5$ (1/mole sec)	
		$C_6H_5SO_3CH_3$	o-$NO_2C_6H_4SO_3CH_3$
$C_6H_5CH_3$ . . .	2.34	1.00	109
C_6H_5Br	5.66	2.07	285
$C_6H_5NO_2$ . . .	35.5	6.75	267
CH_3CN	38.8	8.77	347

We see from Table 2 that the advantage of the methyl esters of nitrobenzenesulfonic acids is retained even in highly polar solvents.

The question of the influence of the structure of the alcoholic residue in esters of arylsulfonic acids on their reactivity has not hitherto received much attention [10]. We investigated the influence of chain length in the alkyl of the ester and the increase in steric hindrance in the amine on the rate of formation of the quaternary salt. The velocity constants at 90° for the reactions that we studied are presented in Table 3.

TABLE 3

Alkylating agent	Reaction with		Solvent	K_1/K
	2-methylbenzothiazole $K_1 \cdot 10^5$ (1/mole sec)	2-isopropylbenzothiazole $K_2 \cdot 10^5$ (1/mole sec)		
$C_6H_5SO_3CH_3$	10.6	3.2	C_6H_5Br	3.3
$C_6H_5SO_3CH_2CH_3$	0.39	0.13	C_6H_5Br	3.0
$C_6H_5SO_3CH_2CH_2CH_3$	0.10	0.0024	C_6H_5Br	4.0
2,4-$(NO_2)(Cl)C_6H_3SO_3CH_3$	645	229	$C_6H_5CH_3$	2.8
2,4-$(NO_2)(Cl)C_6H_3SO_3CH_2CH_3$ . . .	21.8	6.0	$C_6H_5CH_3$	3.6
2,4-$(NO_2)(Cl)C_6H_3SO_3CH_2CH_2CH_3$ . .	8.4	2.8	$C_6H_5CH_3$	3.0

We see from the data of Table 3 that the fall in reaction velocity for one and the same base in passing from methyl esters to their higher homologs is approximately the same for esters of both of the acids considered. Consequently the esters of nitrobenzenesulfonic acids with higher alcohols as alkylating agents retain their superiority over the corresponding esters of benzenesulfonic acids. Steric hindrance in the amine undergoing alkylation has an identical effect in the reaction with esters of benzenesulfonic acid and with esters of nitrobenzenesulfonic acid.

The solubility of the resultant salt frequently exerts a marked influence on the alkylation of tertiary amines with esters of arylsulfonic acids. If the salt is soluble in water, it can easily be separated from solution in the form of the chloride, bromide, iodide or perchlorate by simple addition to the solution of the appropriate halides. In Table 4 are given the solubilities in water of four quaternary salts of 2-methylbenzothiazole.

TABLE 4

Anion of salt	Salt solubility in 100 ml H_2O at 20° (g)
o-$NO_2C_6H_4SO_3^-$	127
m-$NO_2C_6H_4SO_3^-$	85
p-$NO_2C_6H_4SO_3^-$	13
2,4-$(NO_2)(Cl)C_6H_3SO_3^-$.	5.2

Quaternary salts of heterocyclic bases with anions of dinitrobenzenesulfonic acids are poorly soluble in water, and this sometimes hinders their further utilization.

The preparative value of esters of nitrobenzenesulfonic acids may be illustrated by a series of examples. Heating of 2-methyl-6-nitrobenzothiazole with esters of benzenesulfonic acid, starting from the n-propyl ester, leads to low yields or even to non-formation of the quaternary salts. The same base with the corresponding esters of o-nitro- and 2-nitro-4-chlorobenzenesulfonic acid forms quaternary salts with very much greater facility and in higher yields. Comparative data are presented in Table 5.

TABLE 5

Alkylating agent	Duration of heating	Temperature	Yield of quaternary salt (%)
$C_6H_5SO_3CH_3$	5 hours	140–150°	91
$C_6H_5SO_3C_2H_5$	5 "		69
$C_6H_5SO_3C_3H_7$-n.	5 "		18
$C_6H_5SO_3C_3H_7$-iso	5 "		Traces
$C_6H_5SO_3C_4H_9$-n	5 "		13
$C_6H_5SO_3C_5H_{11}$-iso	5 "		Traces
o-$NO_2C_6H_4SO_3CH_3$	10 minutes	100°	94
2,4-$(NO_2)(Cl)C_6H_3SO_3C_2H_5$	10 "		93.5
2,4-$(NO_2)(Cl)C_6H_3SO_3C_3H_7$-n	1 hour		79
2,4-$(NO_2)(Cl)C_6H_3SO_3C_3H_7$-iso . . .	1 "		Traces
o-$NO_2C_6H_4SO_3C_4H_9$-n	1.5 hours		53
o-$NO_2C_6H_4SO_3C_5H_{11}$-iso	2 "		43

If a weak base is thermally unstable, it can frequently not be methylated even with the help of the usual alkylating agents. At the same time, esters of nitrobenzenesulfonic acids, which react at a lower temperature, can give excellent yields in such cases. 2-Methyl-6-nitrobenzothiazole [11] is not stable at above 80°. It does not give quaternary salts either with esters of p-toluenesulfonic acid or with dimethyl sulfate. The quaternary salt was obtained in 18% yield by heating with the methyl ester of o-nitrobenzenesulfonic acid in nitrobenzene solution at 65° for 2 hours. The reaction went at room temperature with the methyl ester of o-nitrobenzenesulfonic acid, and after 24 hours the quaternary salt was isolated in 72% yield. 3-Methyl-2,4-benzothiazole is a weak and unstable base from which no quaternary salts could hitherto be obtained [12]. A quaternary salt was obtained in 57% yield with the methyl ester of 2,4-dinitrobenzenesulfonic acid after heating on a water bath for 20 minutes. Previously unknown cyanine dyes were synthesized from this quaternary salt. An equally weak base is 3-methyl-1,4-benzoxazine [13], which only gives a resin when heated with dimethyl sulfate. A quaternary salt can be prepared from this base by heating with the methyl ester of o-nitrobenzenesulfonic acid at 75°. Cyanine dyes were synthesized from this salt.

Formation of quaternary salt from a tertiary amine and an alkyl halide or ester of a sulfonic acid is a reversible reaction. At high temperature the quaternary salt, especially salts of weak bases, are decomposed into their components. Some weak bases, even of high thermal stability, do not form quaternary salts if high temperatures are employed. Thus, 2-chlorobenzothiazole does not form a quaternary salt when heated with the methyl ester of o-nitrobenzenesulfonic acid at 130° for 5 hours. On the other hand the quaternary salt is obtained in quantitative yield by heating with the methyl ester of 2,4-dinitrobenzenesulfonic acid at 90° for 20 minutes.

Some of our experiments gave negative results. We did not succeed in preparing quaternary salts from 2-methylbenzothiazole with cyclohexyl esters of nitro- and dinitrobenzenesulfonic acids. These esters broke down to cyclohexene and arylsulfonic acid. Negative results were also obtained in an attempt to synthesize a quaternary salt with an aryl radical at the nitrogen atom from γ-picoline by heating it with phenyl or o-nitrophenyl esters of 2,4-dinitrobenzenesulfonic acid.

EXPERIMENTAL

Determination of the velocity constants of methylation of 2-methylbenzothiazole with different methylating agents. The toluene used as solvent was twice distilled in a column (b. p. 110.8°) and stored over sodium. The methyl iodide had b. p. 42.4°. The dimethyl sulfate was distilled in vacuum and treated with magnesia; b. p. 150° (15 mm). 2-Methylbenzothiazole was prepared by condensation of o-aminothiophenol with acetic anhydride. The product was twice distilled in vacuum. B. p. 118° (5 mm).

Experiments were performed by the following standard method: solutions of 2-methylbenzothiazole and alkylating agent were separately prepared in a graduated vessel. Definite volumes of solutions of 2-methylbenzothiazole and alkylating agent were mixed in a test tube with a ground-glass stopper. The test tube was weighed in advance on an analytical balance. Sealed ampoules were used in the experiments with methyl iodide. The test tube containing the mixture was heated for a definite period in a thermostat (temperature fluctuations not exceeding +0.05°); it was then cooled in ice, the quaternary salt was quickly filtered on a weighed glass filter and dried to constant weight at 100°. The test tube containing the residue of quaternary salt was also dried and the weight of residue was added to the weight on the filter. Products obtained with new alkylating agents were analyzed for nitrogen content. Results of analyses and melting points of quaternary salts of 2-methylbenzothiazole with different anions are given in Table 6.

TABLE 6

Anion of the quaternary salt	Melting point	Nitrogen content (%)	
		Found	Calculated
p-$NO_2C_6H_4SO_3^-$	176°	7.82, 7.70	7.65
m-$NO_2C_6H_4SO_3^-$ . . .	169	7.60, 7.66	7.65
o-$NO_2C_6H_4SO_3^-$	110—112	7.45, 7.54	7.65
2,4-$(NO_2)(Cl)C_6H_3SO_3^-$	151—152	7.06, 7.13	6.99
2,4-$(NO_2)(CF_3)C_6H_3SO_3^-$	164—165	6.63, 6.67	6.41
3,4-$(NO_2)_2C_6H_3SO_3^-$ . .	147—148	10.26, 10.28	10.22
3,5-$(NO_2)_2C_6H_3SO_3^-$ . .	170—171	10.08, 9.95	10.22
2,5-$(NO_2)_2C_6H_3SO_3^-$ . .	176—178	10.19, 10.38	10.22
2,4-$(NO_2)_2C_6H_3SO_3^-$ . .	198—199	10.05, 10.01	10.22
2,3-$(NO_2)_2C_6H_3SO_3^-$ . .		9.98, 10.19	10.22

4-5 test tubes were kept in the thermostat for different periods in the case of each alkylating agent at each experimental temperature. The relative error in the analytical determinations did not exceed the error in weighing due to the negligible solubility of the quaternary salt under the experimental conditions. A more serious effect on the accuracy of measurements was the error in timing the treatment of the individual samples, i.e., while the duration of an experiment was 2 hours, the cooling of the sample and the filtration of the precipitate required 1-1.5 minutes. Thus the relative error in time could reach 2%. The volumetric expansion of the solutions was taken into account when calculating the original concentration of substances in the mixture. Since the initial concentration of solutions was small, the coefficient of volumetric expansion of the solutions was assumed equal to the coefficient of volumetric expansion of tuolene.

The velocity constants were determined from the equations for bimolecular reactions. With equal initial concentrations of reactants in accordance with the equation for a second-order reaction, the relation between the function $(1/(a-x)$ (a is the initial concentration, x is the concentration at the end of time t) and time is represented by a straight line, as shown for some of our expts. In Figs. 1 and 2. Deviations in the values of constants calculated for each individual experiment amounted on the average to 3-5%. Since the kinetic experiments with esters of dinitrobenzesulfonic acids were carried out at lower temperatures than the experiments with other alkylating agents, the values of the velocity constants at higher temperatures were found by graphical extrapolation using the Arrhenius equation: $\log K = B - A \cdot \frac{1}{T}$.

The extrapolation for the reaction of 2-methylbenzothiazole with the methyl ester of 2,4-dinitrobenzenesulfonic acid is shown in Fig. 3.

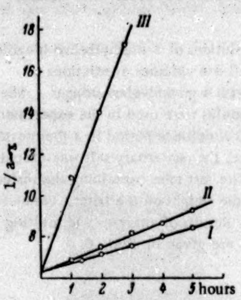

Fig. 1. Velocity of methylation of 2-methylbenzothiazole at 70°.
I - methyl p-nitrobenzenesulfonate;
II - with methyl m-nitrobenzenesulfonate;
III - with methyl o-nitrobenzenesulfonate.

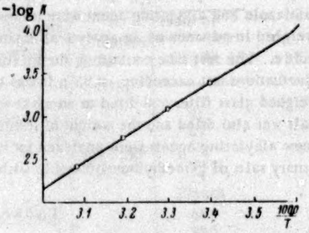

Fig. 3. Temperature dependence of the velocity constant of methylation of 2-methylbenzothiazole with methyl 2,4-dinitrobenzenesulfonate.

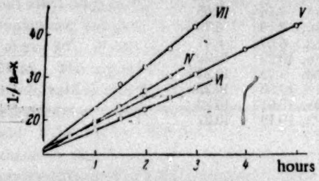

Fig. 2. Velocity of methylation of 2-methylbenzothiazole.
IV - with methyl 2,4-nitrochlorobenzenesulfonate at 70°;
V - with methyl-3,5-dinitrobenzenesulfonate at 70°;
VI and VII - with methyl 2,5-dinitrobenzenesulfonate at 40 and 50°.

Determination of the velocity constants of alkylation of 2-alkylbenzothiazoles with esters of benzenesulfonic acid and esters of 2,4 nitrochlorobenzenesulfonic acid. 2-Isopropylbenzothiazole was prepared by condensation of isobutyryl chloride with o-aminothiophenol. B. p. 108° (4 mm).

The same method was used as before except that an approximately equal volume of ether was added prior to filtration of the quaternary salt because the presence of higher alkyls at the nitrogen atom imparts a certain solubility in toluene and bromobenzene to the quaternary salts. They are completely insoluble in ether and they come down quantitatively when ether is added. In the experiments with esters of 2,4-nitrochlorobenzenesulfonic acid, in which more dilute solutions were used, the coefficient of volumetric expansion of the solutions was assumed equal to that of the solvent. In experiments with esters of benzenesulfonic acid, in which more concentrated solutions were used, the coefficient of volumetric expansion of the solutions was measured with the help of a dilatometer.

Determination of the velocity constants of methylation of 2-methylbenzothiazole in different solvents. The solvents — bromobenzene, nitrobenzene and acetonitrile — were dried over calcium chloride and distilled. When using nitrobenzene and acetonitrile, the mixture was mixed with ether prior to filtration of the quaternary salt in order to completely precipitate the quaternary salt which is partially soluble in nitrobenzene and acetonitrile. Solutions were used with relatively low starting concentrations of reactants (0.3 mole), and the reaction was carried out to the extent of not more than 50% in order to avoid possible complications (catalytic influence of the quaternary salt, etc.). Experiments with the methyl ester of benzenesulfonic acid were run at 70°, those with the methyl ester of o-nitrobenzenesulfonic acid in nitrobenzene and acetonitrile at lower temperatures. In the latter case the temperature coefficient of the reaction was determined, and the velocity constant at 70° was calculated by extrapolation. The coefficient of volumetric expansion was assumed equal to that of the solvents.

Preparation of quaternary salts of weak bases. Synthesis of dyes from them. 2-Methyl-6-nitrobenzothiazole was prepared by nitration of 2-methylbenzothiazole [14]. Alkylation was performed by the following standard method: 0.291 g 2-methy-6-nitrobenzothiazole was heated with an equimolar amount of alkylating agent; the mixture was then extracted with 10 ml boiling water, the solution was filtered from insoluble residue, and the quaternary salt was separated from the filtrate in the form of the iodide after addition of aqueous potassium iodide. The product was washed with a little water, then with alcohol and with ether, and dried.

3-Methyl-2,4-benzothiazine was synthesized as previously described [15], m. p. 42-43°. 0.815 g of the substance was heated with 1.31 g methyl ester of 2,4-dinitrobenzenesulfonic acid in presence of a few drops of toluene on a water bath for 20 minutes. In the absence of a solvent, spontaneous heating occurs and the product partly resinifies. Yield 1.95 g (92%); 2 crystallizations from acetic anhydride gave 1.2 g (57%) with m. p. 144°.

Found %: N 10.03, 9.88. $C_{16}H_{15}O_7S_2N_3$. Calculated %: N 9.88.

Quaternary salts of 3-methyl-2,4-benzothiazine decompose when brought into contact with water.

3-(p-Dimethylaminostyryl)-2,4-benzothiazine methiodide. 0.25 g 3-methyl-2,4-benzothiazine, 0.33 g methyl o-nitrobenzenesulfonate and 10 drops toluene were heated at 100° for 10 minutes. The resultant reddish, thick oil was washed with ether and the so-obtained quaternary salt was used for the preparation of a dye without further purification. To its solution in 3 ml acetic anhydride was added 0.25 g p-dimethylaminobenzaldehyde, and the mixture was heated to the boil for 20 minutes. A dye came down after decomposition of the acetic anhydride with water. It was collected, washed with ether and dissolved in alcohol. The iodide was precipitated by addition of potassium iodide to the alcoholic solution. Yield 0.3 g (45%) of fine needles; maximum of absorption in chloroform at 546 mμ.

Found %: I 29.00, 29.21. $C_{19}H_{21}N_2SI$. Calculated %: I 29.13.

Bis-(4-methyl-2,4-benzothiazine-3)-trimethylcyanine perchlorate. The quaternary salt prepared from 0.12 g methylbenzothiazine and 0.17 g methyl o-nitrobenzenesulfonate was heated with 0.3 g orthoformic ester, 2 ml acetic anhydride and 0.5 ml pyridine at 100° for 30 minutes. The acetic anhydride was decomposed with water and the resultant product was dissolved in a mixture of methyl alcohol and water and precipitated with sodium perchlorate. Fine bronze needles. Yield 0.03 g (17%); absorption maximum in chloroform at 518 m μ.

Found %: Cl 6.90, 6.99. $C_{12}H_{21}O_4N_2S_2Cl$. Calculated %: Cl 7.53.

Methyl-2,4-dinitrobenzenesulfonate of 2-chlorobenzothiazole was prepared by heating 0.17 g 2-chlorobenzothiazole and 0.26 g methyl ester of 2,4-dinitrobenzenesulfonic acid at 90° for 20 minutes. Decomp. temperature 162-163° (from acetic anhydride); yield nearly quantitative.

Found %: N 9.38, 9.45. $C_{12}H_{10}O_7N_3S_2Cl$. Calculated %: N 9.75.

The product decomposes when heated with water and evolves hydrogen chloride.

3-Methyl-1,4-benzoxazine was synthesized as previously described [13]. Its quaternary salt was obtained from 0.22 g base and the equimolar amount (0.32 g) of methyl o-nitrobenzenesulfonate at 75° after 5 minutes. The dark, viscous oil was washed with benzene and ether; it crystallized after a few days. The quaternary salt was used for the preparation of dyes without further purification.

3-(p-Dimethylaminostyryl)-1,4-benzoxazine methoperchlorate. The above quaternary salt was heated with the equimolar amount of p-dimethylaminobenzaldehyde and 2 ml acetic anhydride on a water bath for 10 minutes. The dye was precipitated with ether, dissolved in alcohol and treated with sodium perchlorate. Crystallization from alcohol gave 0.1 g dark-blue crystals with an absorption maximum in chloroform at 564 m μ.

Found %: N 7.15, 7.13. $C_{19}H_{21}O_5N_2Cl$. Calculated %: N 7.13.

(3-Methylbenzothiazole-2)-(4-methyl-1,4-benzoxazine-3)-monomethinecyanine perchlorate was prepared from 0.55 g methyl o-nitrobenzenesulfonate of 3-methyl-1,4-benzoxazine and 0.46 g methylmethosulfate of 2-methylmercaptobenzothiazole in alcohol with addition of anhydrous sodium acetate by heating at 100° for 1 hour. The dye was brought down with sodium perchlorate and recrystallized from alcohol. Fine red crystals; yield 0.1 g; absorption maximum in chloroform at 432 mμ.

Found %: N 6.74, 6.90. $C_{18}H_{17}O_5N_2SCl$. Calculated %: N 6.85.

Methyl o-nitrobenzene sulfonate of 2-methyl-6-nitrosobenzothiazole was obtained by heating a mixture of equimolar amounts of 2-methyl-6-nitrosobenzothiazole [11] and methyl o-nitrobenzenesulfonate at 65° for 2 hours (in nitrobenzene solution). The solid product was washed with benzene and ether, dissolved in hot water and precipitated with sodium perchlorate. Yield of salt 0.06 g (18%) (from water).

Found %: N 9.54, 9.67. $C_9H_9O_5N_2SCl$. Calculated %: N 9.57.

The quaternary salt of the same base with methyl 2,4-dinitrobenzenesulfonate in nitrobenzene was obtained in 72% yield after standing for several days at room temperature.

Found %: N 12.30. 12.06. $C_{15}H_{12}O_8N_4S_2$. Calculated %: N 12.73.

2-p-Dimethylaminostyryl-6-nitrosobenzothiazole methoperchlorate. 0.094 g 2-methyl-6-nitrosobenzothiazole methoperchlorate and 0.049 g p-dimethylaminobenzaldehyde were heated with 5 ml acetic anhydride at 100° for 40 minutes. Yield of dye 0.1 g; absorption maximum in alcohol at 563 m μ.

Found %: N 9.97, 9.88. $C_{18}H_{18}O_5N_3SCl$. Calculated %: N 9.92.

SUMMARY

A study was made of the velocity of formation of quaternary salts from 2-methylbenzothiazole with methyl iodide, dimethyl sulfate and the methyl esters of 12 arylsulfonic acids: benzenesulfonic acid; o-, m- and p-nitro-benzenesulfonic acids; 2,3-, 2,4-, 2,5-, 3,4- and 3,5-dinitrobenzenesulfonic acids; 2-nitro-4-chlorobenzenesulfonic acid and 2-nitro-4-trifluoromethylbenzenesulfonic acid. The methyl ester of o-nitrobenzenesulfonic acid is shown to be 6 times and the methyl esters of 2,3- and 2,4 - dinitrobenzenesulfonic acids about 60 times more active than dimethyl sulfate. Application of esters of nitrobenzenesulfonic acids enables the preparation of quaternary salts under milder conditions and in better yields than had previously been possible. It is feasible to synthesize quaternary salts of those weak bases which never form quaternary salts with other alkylating agents. The employment of esters of nitrobenzenesulfonic acid is illustrated by the formation of quaternary salts of 2-methyl-6-nitro-, 2-methyl-6-nitroso- and 2-chlorobenzothiazoles, 3-methyl-2,4-benzothiazine and 3-methyl-1,4-benzoxazine.

LITERATURE CITED

[1] N. Menshutkin, J. Russ. Phys.-Chem. Soc. 22, 346, 393 (1890).

[2] F. Ullmann and P. Wenner, Ber. 33, 2476 (1900).

[3] V. M. Rodionov, Bull. soc. chim. 45, 109, 121, (1929).

[4] J. Kastle and P. Murrill, Am. Chem. J. 17, 290, (1895).

[5] M. Boyle, J. Chem. Soc. 97, 211 (1910).

[6] L. Demeny, Rec. trav. chim. 50, 60 (1931).

[7] M. Morgan and L. Cretcher, J. Am. Chem. Soc. 70, 375 (1948); E. Tommila and M. Lindholm, Acta Chem. Scand. 5, 647 (1951); C. A. 46, 7413 (1952); R. Robertson, Can. J. Cem. 31, 589 (1953); C. A. 47, 12283 (1953).

[8] N. Menshutkin, J. Russ. Phys.-Chem. Soc., 22, 393 (1890).

[9] S. Palit, J. Org. Ch., 12, 752 (1947).

[10] R. Robertson, Can. J. Chem. 31, 589 (1953).

[11] A. Kiprianov and I. Fedorova, Ukrain. Chem. J. 21, 78 (1955).

[12] B. Beilenson, F. Hamer, J. Chem. Soc., 1942, 98.

[13] R. Störmer, H. Brockerhof, Ber., 30, 1641 (1897).

[14] A. Kiprianov and E. Sych, Trans. Inst. Chem. Kharkov State Univ. 2, 16 (1936).

[15] B. Beilenson, F. Hamer and R. Rathbone, J. Chem. Soc. 1945, 222.

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Institute of Organic Chemistry,
Academy of Sciences, Ukrainian SSR

SUMMARY

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LITERATURE CITED

[1] [illegible]

[2] [illegible]

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[4] [illegible]

[5] [illegible]

[6] [illegible]

[7] [illegible]

[8] [illegible]

[9] [illegible]

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[11] [illegible]

[12] [illegible]

[13] [illegible]

[14] [illegible]

[15] [illegible]

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INTERACTION OF PHOSPHORUS PENTACHLORIDE WITH SOME HALOGENATED OLEFINS

Yu. M. Zinovyev, V. N. Kulakova and L. Z. Soborovsky

The formation of organophosphorus compounds by reaction of phosphorus pentachloride with unsaturated hydrocarbons has been repeatedly observed [1-5]. Propylene, butylene and isobutylene are among the simplest olefins brought into reaction. The corresponding phosphorus chloroalkyltetrachlorides are formed:

$$RCH{=}CH_2 + PCl_5 \rightarrow RCHClCH_2PCl_4.$$

It was recently shown that phosphorus pentachloride readily adds on to vinyl ethers [6]. These reactions are usually performed at 20° in a benzene medium. We studied the possibility of adding on phosphorus pentachloride to some chlorosubstituted olefins (vinyl chloride, vinylidene chloride and allyl chloride). When the reaction is conducted under the mild conditions described above, phosphorus pentachloride substantially does not interact with the above-mentioned chloroolefins (only traces of the corresponding products of chlorination at the double bond are isolated). Under more drastic conditions (heating to 110° under pressure without a solvent) phosphorus pentachloride entered almost completely into reaction. Even then, however, no organophosphorus compounds were detected in the reaction mass. Reaction of vinyl chloride with phosphorus pentachloride gave, apart from unchanged olefin, phosphorus trichloride, 1,1,2-trichloroethane (product of chlorination of vinyl chloride at the double bond) and a chlorinated hydrocarbon with twice the number of carbon atoms which proved to be the previously unknown 1,1,4,4-tetrachlorobutane. The yield of trichloroethane was 31%, that of tetrachlorobutane 33.6%, reckoned on the vinyl chloride converted. Similarly, allyl chloride gave, apart from 1,2,3-trichloropropane, 1,2,5,6-tetrachlorohexane. Formation in this reaction of products of chlorination at the double bond is readily accounted for by the chlorinating action of phosphorus pentachloride which proceeds according to the scheme:

$$RCH{=}CH_2 + PCl_5 \rightarrow RCHClCH_2Cl + PCl_3.$$

We cannot so readily account for the appearance of polychloroalkanes with double the number of carbon atoms. One possibility is dimerization of the reacting chloroolefins at higher temperature followed by chlorination of the corresponding dimers. Another possibility is free-radical chlorination of the original compounds. For clarification of the mechanism of formation of polychloroalkanes, vinyl chloride was heated under pressure both alone and in admixture with sulfuryl chloride; the chlorinating properties of the latter are similar to those of phosphorus pentachloride.* In neither case, however, was a compound obtained whose chain length exceeded that of the original substance.

We suggest that the above polychloroalkanes with double the number of carbon atoms are formed via the addition of phosphorus pentachloride to the olefin molecule with formation of the corresponding chloroalkyltetrachloride of phosphorus. In the case of vinyl chloride the reaction is expressed by:

$$CH_2{=}CHCl + PCl_5 \rightarrow CHCl_2CH_2PCl_4.$$

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* An example has been reported [7] of the preparation of polychlorinated butane by treatment of vinyl chloride with sulfuryl chloride in presence of pyridine. Here the decisive factor was the presence of pyridine.

The phosphorus chloroalkyltetrachloride then breaks down with formation of molecules containing twice the number of carbon atoms and 1,1,2-trichloroethane:

$$2CHCl_2CH_2PCl_4 \rightarrow CHCl_2CH_2CH_2CHCl_2 + PCl_5 + PCl_3,$$
$$CHCl_2CH_2PCl_4 \rightarrow CHCl_2CH_2Cl + PCl_3.$$

The possibility of formation of such polychloroalkanes with twice the number of carbon atoms from phosphorus chloroalkyltetrachlorides is illustrated by the thermal decomposition of phosphorus 2-chloropropyltetrachloride, obtained from propylene and phosphorus pentachloride. Heating of this tetrachloride in an autoclave to 100-110° gives a small amount of tetrachlorohexane, apart from phosphorus trichloride, 1,2-dichloropropane and hydrogen chloride. The tetrachlorohexane could originate from chlorination of the alkyl residue at the phosphorus, rupture of the C-P bond and combination of the resultant radicals to form a molecule with double the length of carbon chain:

$$2CH_3CHClCH_2PCl_4 \rightarrow C_3H_5Cl_2PCl_4 + CH_3CHClCH_2Cl + PCl_3 + HCl.$$
$$2C_3H_5Cl_2PCl_4 \rightarrow C_6H_{10}Cl_4 + PCl_3 + PCl_5.$$

On the basis of this hypothesis we may represent the reaction of allyl chloride with phosphorus pentachloride by the following scheme:

$$CH_2ClCH{=}CH_2 + PCl_5 \longrightarrow CH_2ClCHClCH_2Cl + PCl_3,$$
$$CH_2ClCH{=}CH_2 + PCl_5 \longrightarrow CH_2ClCHClCH_2PCl_4,$$
$$CH_2ClCHClCH_2PCl_4 \longrightarrow CH_2ClCHClCH_2Cl + PCl_3,$$
$$2CH_2ClCHClCH_2PCl_4 \longrightarrow CH_2ClCHClCH_2CH_2CHClCH_2Cl + PCl_3 + PCl_5,$$
$$CH_2ClCHClCH_2PCl_4 + PCl_3 \longrightarrow CH_2ClCHClCH_2Cl + PCl_3 + PCl_5.$$

Under the same conditions vinylidene chloride is completely transformed into a solid polymer.

Examination of the configuration of the tetrachlorobutane isolated in the present work indicates the possibility of existence of 14 structures. Formation of 8 structures containing unsubstituted methyl groups may, however, be ruled out. Another improbable isomer is 1,1,1,4-tetrachlorobutane which contains the CCl_3 group. 1,2,3,4-Tetrachlorobutane has been described [8], but its constants [m. p. 73°, b. p. 130-140° (50 mm)] differ markedly from those found for the substance isolated. Consequently 4 probable structures remain: 1, 1,4,4-, 1,2,2,4-, 1,1,2,4- and 1,1,3,4-tetrachlorosubstituted butanes. Selection of the most probable structure was based on examination of the products of dehydrochlorination of the tetrachlorobutane. Treatment of the tetrachlorobutane with alcoholic alkali leads to cleavage of either one molecule of hydrogen chloride with formation of trichlorobutene or of two molecules with formation of dichlorobutadiene. The properties of both of the chloroolefins obtained differ from the properties of known trichlorobutenes and dichlorobutadienes. The structures of the previously unknown 1,4-dichlorobutadiene-1,3 and 1,1,4-trichlorobutene-3 may therefore be assigned to the unsaturated chloroderivatives obtained, and the reactions with caustic alkali can be represented by the following equations:

$$CHCl_2CH_2CH_2CHCl_2 + KOH \rightarrow CHCl = CHCH_2CHCl_2 + KCl + H_2O,$$

$$CHCl_2CH_2CH_2CHCl_2 + 2KOH \rightarrow CHCl = CHCH{=} CHCl + 2KCl + 2H_2O.$$

The occurrence of an exaltation of molecular refraction of the prepared dichlorobutadiene confirms that it is 1,4-dichlorobutadiene-1,3.

Further confirmation of the structure of the dichlorobutadiene was obtained by plotting the infrared absorption spectrum*. In accord with the formulas (I) and (II) possible for a substance with the composition

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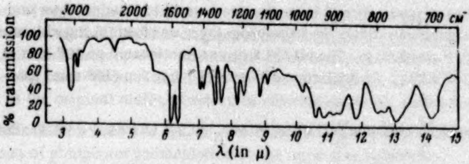
* Spectrographic investigation by S.S. Dubov and V. I. Fedotova.

$CHCl{=}CH{-}CH{=}CHCl$ (I) $CHCl{-}CH{=}CH{-}CHCl$ (II) $CH_2Cl{-}C{\equiv}C{-}CH_2Cl.$ (III)



Infrared absorption spectrum of 1,4-dichlorobutadiene-1,3 (layer thickness 0.3 mm).

we should expect to find an absorption band in the 1600 cm^{-1} region, which is characteristic of the valence vibrations of the C=C bond. Actually a double band with absorption maxima at 1622 and 1562 cm^{-1} is found in this region. The doublet character of this band, its high intensity and its slightly lower position in relation to the vibration frequencies of a single C=C bond are characteristic of compounds containing conjugated C=C bonds [9]. All this supports structure (I). A structure corresponding to formula (III) should be characterized by the presence in the infrared spectrum of a band in the 2000-2200 cm^{-1} region (C≡C bond). The region in question does not contain a strong band characteristic of this bond.

Formation of 1,4-dichlorobutadiene-1,3 is possible only from two isomers of tetrachlorobutane whose presence in the obtained substance is probable — 1,1,1,4- and 1,1,3,4-tetra- derivatives. Consideration, however, of the above scheme of formation of this substance from vinyl chloride strengthens the view that the compound isolated is 1,1,4,4-tetrachlorobutane.

EXPERIMENTAL

Reaction of vinyl chloride with phosphorus pentachloride

Reaction at atmospheric pressure at 20° in a benzene medium. Dry vinyl chloride was passed for 15 hours through a suspension of 52 g phosphorus pentachloride in 300 ml benzene. Sulfur dioxide was then passed through the reaction mixture in order to convert the solid phosphorus alkyltetrachloride and phosphorus pentachloride into the distillable acid chloride of chloroethanephosphinic acid. Passage of sulfur dioxide was continued until the solution was homogeneous. On distillation the whole of the liquid came over up to 114°. The 100-114° fraction, consisting mainly of phosphorus oxychloride, was treated with water. The residual oil (about 1 g) was washed, dried over calcium chloride and distilled. B. p. 112-113°; d_4^{20} 1.4403. The boiling point of 1,1,2-trichloroethane is 113.7°, d_4^{20} 1.4416 [10].

Reaction by heating under pressure. a) 208 g phosphorus pentachloride was charged into an autoclave of special steel, the autoclave was cooled to -70° and 100 g vinyl chloride was condensed into it. The autoclave was heated for 12 hours at 110°. The pressure at the start rose to 20 atm. and then fell to 14 atm. After cooling, unreacted vinyl chloride (27.8 g) was released from the autoclave. The weight of the residual liquid was 264.3 g. It was fractionated. 161.3 g (mixture of phosphorus trichloride and 1,1,2-trichloroethane) came over at 70-115°. From this fraction was isolated 48.0 g (31 %) 1,1,2-trichloroethane. Further distillation was carried out in vacuum and the following fractions were obtained: 30-90° (1 mm) 58.9 g, 90-125° (1 mm), 15.0 g; residue 10.0 g. Redistillation of the 30-90° fraction gave 37.8 g (33.6%) of 1,1,4,4-tetrachlorobutane.

B. p. 52-54° (1 mm) or 200° (745 mm); d_4^{20} 1.4477, n_D^{20} 1.4995, MR_D 39.84; Calculated 40.14. Found %: C 24.82, 25.14; H 3.57, 3.20; Cl 73.02, 72.16, M 196, $C_4H_6Cl_4$. Calculated %: C 24.52; H 3.09; Cl 72.39. M 195.93.

b) 35 g vinyl chloride and 62 g sulfuryl chloride were heated for 15 hours at 110° in a steel tube fitted with a pressure gage. The pressure reached 11 atm. Unreacted vinyl chloride was removed from the tube after cooling. From the liquid reaction mass was isolated 11 g (18%) 1,1,2-trichloroethane.

Dehydrochlorination of tetrachlorobutane

20 g tetrachlorobutane with b. p. 200° was added with cooling and stirring to a solution of 13 g potassium hydroxide in 60 ml alcohol. After 2 hours the mass was diluted with water and the oily layer was collected and dried over magnesium sulfate. In the aqueous layer was found 6.2 g chlorine. The amount of chlorine theoretically split off was 7.25 g. The oil (13.2 g) was fractionated at 108 mm to give: 54-67° 4.15 g; 67-90° 1.65 g; 95-132° 4.99 g. Redistillation of the 54-67° fraction (108 mm) gave 2.0 g of 1,4-dichlorobutadiene-1,3.

B. p. 54-55° (104 mm), d_4^{20} 1.2087, n_D^{20} 1.5118, * MR_D 30.58; Calculated 29.47; EMR_D 1.11.

Found %: C 38.72, 38.67; H 3.41, 3.88. M 125. $C_4H_4Cl_2$. Calculated %: C 39.05; H 3.28. M 122.99.

Redistillation of the 95-132° (108 mm) fraction gave 1,1,4-trichlorobutene-3.

B. p. 101° (38 mm), d_4^{20} 1.3530, n_D^{20} 1.4960, MR_D 34.66; Calculated 34.81.

Found %: C 29.52, 29.65; H 3.83, 3.80. M 168. $C_4H_5Cl_3$. Calculated %: C 30.12; H 3.16, M 159.46.

Reaction of allyl chloride with PCl_5.

a) A mixture of 38.3 g allyl chloride, 104 g phosphorus pentachloride and 120 g dry benzene was stirred for 12 hours at 20°. Through the reaction mixture was then passed sulfur dioxide until the solid products had dissolved. On distillation, the liquid came over completely up to 115°.

b) 16.3 g allyl chloride and 50 g phosphorus pentachloride was heated in a closed steel tube for 14 hours at 120-130°. After cooling, the reaction mixture was a homogeneous liquid. The following fractions were collected from 54.1 g mixture: 45-155° 43.7 g; 155-158° 2.8 g; 50-120° (16 mm) 1.3 g; 120-130° (16 mm) 1.4 g. The boiling point of 1,2,3-trichloropropane is 158°; the remaining isomers (1,2,2-, 1,1,3-, 1,1,2- and 1,1,1-trichloropropanes) boil between 123 and 150° [13]. Redistillation of the 120-130° fraction (16 mm) gave 1,2,5,6-tetrachlorohexane.

B. p. 94-100° (2 mm), d_4^{20} 1.4043, n_D^{20} 1.5136, MR_D 49.05; Calculated 49.38.

Found %: C 31.78, 32.08; H 4.10, 4.02. M 213, 224. $C_6H_{10}Cl_4$. Calculated %: C 32.17; H 4.51. M 223.98.

Reaction of vinylidene chloride with phosphorus pentachloride. 55 g vinylidene chloride and 104 g phosphorus pentachloride were heated in a steel tube for 9 hours at 130°. No pressure was registered in the tube. After cooling, the tube contained unchanged phosphorus pentachloride and a solid, white polymer.

Thermal decomposition of phosphorus 2-chloropropyltetrachloride.

Propylene was passed through a suspension of phosphorus pentachloride in benzene at 20° until reaction ceased (change of external form of precipitate). The solvent was then taken off in vacuum and the resultant phosphorus 2-chloropropyltetrachloride (146 g) was heated in a steel autoclave for 10 hours at 100-110°. The pressure in the autoclave rose to 20 atm. After cooling, the pressure fell to 10 atm. The hydrogen chloride formed was absorbed by caustic alkali solution (increase in weight 14.0 g). From the autoclave was extracted 121 g light-brown liquid and a small quantity of dark resin. The main bulk of the liquid consisted of phosphorus trichloride and 1,2,-dichloropropane. The residue was diluted with ether, washed at first with dilute hydrochloric acid (from iron salts), then with sodium carbonate solution and with water, and dried with fused calcium chloride. After removal of ether, the residue was distilled; 0.1 g came over at 30-60° (4 mm)

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* 2,3-Dichlorobutadiene-1,3, an isomer of the compound isolated, has b. p. 39-42° (80 mm), d_4^{20} 1.1820, n_D^{20} 1.4882 [11]. The other isomer — 1,2-dichlorobutadiene-1,3 — has b. p. 60-65° (105 mm), d_4^{20} 1.2070, n_D^{20} 1.5078 [12].

(d_4^{20} 1.4225, n_D^{20} 1.5075) and 0.3 g at 80° (4 mm) (d_4^{20} 1.3829, n_D^{20} 1.5233, MR_D 49.50; calc. 49.38); the latter probably had the structure of 2,2,5,5,-tetrachlorohexane.

Found %: C 32.36, 32.84; H 3.49, 3.56. M 221. $C_6H_{10}Cl_4$. Calculated %: C 32.17; H 4.51. M 223.98.

SUMMARY

1. Treatment of vinyl chloride and allyl chloride with phosphorus pentachloride at 20° in benzene at atmoshperic pressure leads to small yield of only products of addition of chlorine at the double bond (1,1,2-trichloroethane and 1,2,3-trichloropropane). Reaction of phosphorus pentachloride with the same haloolefins with heating to 100-110° under pressure leads to formation of halogenated hydrocarbons containing twice as many carbon atoms as the original olefin. Products of chlorination at the double bond are formed simultaneously.

2. 1,1,4,4-Tetrachlorobutane and 1,2,5,6-tetrachlorohexane are described for the first time. They are obtained by the action of phosphorus pentachloride on the respective haloolefins.

3. Thermal decomposition (at 100-110°) of phosphorus 2-chloro-propyltetrachloride gives, apart from 1,2-dichloropropane, small amounts of a tetrachlorohexane whose structure is probably represented by $CH_3CCl_2CH_2CH_2CCl_2CH_3$.

4. A mechanism for the formation of 1,1,4,4-tetrachlorobutane and 1,2,5,6- and 2,2,5,5-tetrachlorohexanes during the reaction of phosphorus pentachloride with the respective haloolefins is advanced.

5. Dehydrogenation of 1,1,4,4-tetrachlorobutane gives the previously unknown 1,4-dichlorobutadiene-1,3 and 1,1,4-trichlorobutene-3.

LITERATURE CITED

[1] E. Bergmann and A. Bondi, Ber. 63, 1158 (1930); 64, 1455 (1931).

[2] U. S. Patent 2471472; C. A. 43, 7499 (1949); 2495799 C. A. 44, 3517 (1950).

[3] G. Kosolapoff and W. Huber, J. Am. Chem. Soc. 68, 2540 (1946).

[4] G. Kosolapoff and J. McCulough, J. Am. Chem. Soc. 73, 855 (1951).

[5] M. I. Kabachnik, Prog. Chem., 16, 403 (1947).

[6] K. N. Anisimov, N. E. Kolobova and A. N. Nesmeyanov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1954, 610, 796, 799, 803.*

[7] A. Ya. Yakubovich and Yu. M. Zinovyev, J. Gen. Chem. 17, 2028 (1947).

[8] H. Backer and J. Starting, Rec. trav. chim. 54,55 (1935).

[9] L. Bellamy, The Infra-red Spectra Complex Molecules (N.Y., 1954), 35.

[10] H. Prins, Rec. trav. chim. 45, 80 (1926).

[11] A. L. Klebansky, A. P. Belenkaya and K. K. Chevychalova, J. Appl. Chem. 19, 200 (1946).

[12] A. L. Klebansky, L. S. Volkenshtein and A. P. Orlova, J. Gen. Chem. 5, 1255 (1935).

[13] Dictionary of Organic Compounds (1949) Vol. 3.

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d_4^{20} 1.4028, n_D^{20} 1.4979) and 2.3 g of [illegible] (d_4^{20} 1.4306, n_D^{20} [illegible], MR [illegible]). The latter probably had the structure of [illegible].

Found %: C 32.30, 32.44; H 3.40, 3.56; [illegible]. Calculated %: [illegible].

SUMMARY

1. Treatment of vinyl chloride and allyl chloride with phosphorus pentachloride at 20° in benzene at atmospheric pressure leads to [illegible] at the double bond (1,1,2-trichloroethane and 1,2,3-trichloropropane). [illegible] with heating at 100-140° under pressure leads to [illegible] containing twice as many carbon atoms as the original olefin. Products of chlorination at the double bond are formed simultaneously.

2. 1,1,4,4-Tetrachlorobutane and 1,2,3,4-tetrachlorobutane are described for the first time. They are obtained by the action of phosphorus pentachloride on the respective [illegible].

3. Thermal decomposition (at 100-110°) of [illegible] yields, apart from 1,2-dichloropropane, small amounts of a [illegible] whose structure is probably represented by $CH_2ClCH_2CH_2CCl_2CH_3$.

4. A mechanism for the formation of 1,1,4,4-tetrachlorobutane and [illegible] during the reaction of phosphorus pentachloride with the respective [illegible] is advanced.

5. Dehydrogenation of 1,1,4,4-tetrachlorobutane [illegible] and 1,1,4-trichlorobutene-2.

LITERATURE CITED

[1] E. Bergmann and A. Bondi, Ber. 66, 278 (1933); 66, 286 (1933).

[2] [illegible]

[3] G. Kosolapoff and [illegible], J. Am. Chem. Soc. [illegible]

[4] G. Kosolapoff and [illegible], J. Am. Chem. Soc. [illegible]

[5] M. I. Kabachnik, Prog. Chem. 16, [illegible] (1947).

[6] K. N. Anisimov, N. E. Kolobova and A. N. Nesmeyanov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1954, [illegible]*.

[7] A. Ya. Yakubovich and [illegible], J. Gen. Chem. [illegible]

[8] [illegible]

[9] [illegible]

[10] [illegible]

[11] A. L. Klebansky, [illegible], J. Appl. Chem. [illegible]

[12] A. L. Klebansky, [illegible], J. Gen. Chem. [illegible]

[13] Dictionary of Organic Compounds, [illegible]

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SYNTHESIS OF DICHLOROPHENYLTRIACETOXYSILANE AND ITS HYDROXY DERIVATIVES

K. A. Andrianov, A. A. Zhdanov and E. F. Morgunova

In the synthesis of high-molecular organosilicon compounds — polyorganosiloxanes — the hydrolysis of alkylchlorosilanes or similar compounds is a very important reaction. Many papers have been published on this process [1-4] and they draw attention to processes of formation of intermediate products of hydrolysis of the monomeric organosilicon compounds and to their transformations into polymers.

In the past the monomeric organosilicon compounds containing more than one hydroxyl group at the silicon atom have been difficultly accessible substances due to their poor stability. Diethyldihydroxysilane was first isolated in 1946 [5] and dimethyldihydroxysilane in 1953 [6]. Attempts to obtain alkyl-or aryl-trihydroxysilanes were unsuccessful. Hydrolysis of phenyltrimethyloxysilane gave a polymer [6], while hydrolysis of phenyltriacetoxysilane yielded a linear product — 1,2,3-triphenyl-pentahydroxytrisiloxane [4]. In 1955 a method was described [7] for preparing phenyltrihydroxysilane by hydrolysis of phenyltrimethoxysilane. Since the susceptibility to formation of polymers by hydroxyl-containing organosilicon compounds decreases with increasing molecular weight of the organic radical linked to the silicon atom, we should expect alkyltrihydroxysilanes containing an organic radical with a high molecular weight to be sufficiently stable to permit of their isolation.

In the present work we studied the hydrolysis of dichlorophenyltriacetoxysilane. In the hydrolysis of the following compounds with excess of water in presence of ether, we obtained the corresponding hydroxy derivatives according to the reaction schemes:

$$C_6H_3Cl_2SiCl_3 + 3(CH_3CO)_2O \longrightarrow C_6H_3Cl_2Si(OCOCH_3)_3 + 3CH_3COCl,$$

$$2C_6H_3Cl_2Si(OCOCH_3)_3 \xrightarrow{\text{heat}} [(C_6H_3Cl_2)Si(OCOCH_3)_2]_2O + (CH_3CO)_2O,$$

$$C_6H_3Cl_2Si(OCOCH_3)_3 + 3H_2O \longrightarrow C_6H_3Cl_2Si(OH)_3 + 3CH_3COOH,$$

$$[(C_6H_3Cl_2)Si(OCOCH_3)_2]_2O + 4H_2O \longrightarrow [(C_6H_3Cl_2)Si(OH)_2]_2O + 4CH_3COOH.$$

The compounds obtained are crystalline solids, soluble in the majority of polar organic solvents and readily transformed by heating into polymers.

EXPERIMENTAL

Dichlorophenyltriacetoxysilane. A mixture of 207 g dichlorophenyltrichlorosilane (b. p. 260-267° content of hydrolyzable chlorine 36.63 %) and 226 g acetic anhydride was placed in a round-bottomed flask with a reflux condenser and a calcium chloride tube and kept at room temperature for 96 hours. The acetyl chloride that had been formed was then removed in vacuum; the residue in the flask crystallized on cooling. Yield 94.5%. The acetyl group content was 46.15%. The calculated content of acetyl groups in dichlorophenyltriacetoxysilane is 50.42%. The substance was purified by two methods. 30 g was treated with 30 ml ether at room temperature. The insoluble residue (colorless crystals) was filtered, washed the cold with ether and dried in a vacuum-desiccator over calcium chloride. Yield of product

43.3% of the amount taken. In another experiment 205 g of substance was mixed with 205 ml ether and the mixture refluxed until solution was complete; the filtered solution was then cooled with ice. After standing for a few hours at 0°, the crystals were filtered, washed with ether and dried in a vacuum-desiccator. Yield 43.8% of the amount taken. Results are set forth in the table.

Method of purification	Yield %	Melting point	Si content (%)		$OCOCH_3$ content (%)	
In the cold	40.8	68-69°	8.75	7.97	49.42	50.42
With heating	41.4	68-69°	8.19	7.97	50.76	50.42

1,3-Bis-(dichlorophenyl)-tetraacetoxydisiloxane. 207 g dichlorophenyltrichlorosilane and 226 g acetic anhydride were placed in a round-bottomed flask fitted with a dephlegmator. The resultant acetyl chloride was distilled off at about 55° and collected in a receiver. After 100 g acetyl chloride had come over, the residue of acetyl chloride and acetic anhydride was removed in vacuum. The residue in the flask was cooled to room temperature to form a viscous mass which at once crystallized when an attempt was made to pour it out of the flask. For purification, 40 g of product was treated with 40 ml ether; complete solution did not occur even after heating to the boiling point of ether. Purification was accordingly effected by repeated washing with ether. Yield 48 g (21.7%) 1,3-bis-(dichlorophenyl)-tetraacetoxysilane.

Found %: Si 9.73; $OCOCH_3$ 39.25. $C_{20}H_{18}O_9Cl_4Si_2$. Calculated: %: Si 9.33; $OCOCH_3$ 39.33.

Dichlorophenyltrihydroxysilane. 26 g dichlorophenyltriacetoxysilane was dissolved in 156 ml ether. The resultant solution was added to a mixture of 250 g ice and 250 ml water. The aqueous layer was separated from the ether layer and extracted with 75 ml ether. The main layer and the ethereal extract were combined and washed twice with a little water, and the ether was removed by evaporation at room temperature in an air stream. The residual white, pulverulent substance was washed with benzene and dried to constant weight in a vacuum-desiccator. The yield ranged from 15 to 20% and depended upon the duration of hydrolysis and of evaporation of the ether (10-15 minutes). The crystalline product has m. p. 188° (it is simultaneously transformed into polymers), is soluble in acetone, ether and alcohol, insoluble in benzene. The product was analyzed for its content of Si, C, H, Cl and OH. The content of OH groups was determined by dehydration of a weighed sample at about 300° and collection of the water in a calcium chloride tube. Good agreement was found between the increase in weight of the calcium chloride tube and the loss in weight of the boat containing the sample. This shows the absence of pyrolysis at the dehydrating temperature.

Found %: C 32.92; H 2.59; Cl 31.66; Si 12.63; OH 22.21. $C_6H_6O_3Cl_2Si$. Calculated %: C 32.01; H 2.68; Cl 31.50; Si 12.46; OH 22.67.

1,3-Bis-(dichlorophenyl)-tetrahydroxydisiloxane was prepared similarly from 5 g 1,3-bis-(dichlorophenyl)-tetraacetoxydisiloxane. Crystals with m. p. 155° soluble in alcohol, ether and acetone, insoluble in benzene.

Found %: C 31.18; H 3.19; Si 13.01; OH19.25. $C_{12}H_{10}O_5Cl_4Si_2$. Calculated %: C 33.35; H 2.33; Si 12.98; OH 15.74.

The product is probably contaminated with 1,3-bis-(dichlorophenyl)-tetrahydroxydisiloxane. Only polymers were isolated when an attempt was made to purify it by recrystallization after redissolution.

SUMMARY

1. The reaction of dichlorophenyltrichlorosilane with acetic anhydride was investigated, and the reaction was used as a basis for the synthesis for the first time of dichlorophenyltriacetoxysilane and 1,3-bis-(dichlorophenyl)-tetraacetoxysilane.

2. Hydrolysis of dichlorophenyltriacetoxysilane gave monomeric dichlorophenyltrihydroxysilane, an

intermediate product in the formation of organosilicon polymers by the hydrolysis reaction.

LITERATURE CITED

[1] K. A. Andrianov and N. N. Sokolov, Proc. Acad. Sci. USSR 82, 909 (1952).

[2] K. A. Andrianov and N. N. Sokolov, Proc. Acad. Sci. USSR 101, 81 (1955).

[3] F. Patnode and D. Wilcock, J. Am. Chem. Soc. 68, 358 (1946).

[4] K. A. Andrianov and A. A. Zhdanov, Bull. Acad. Sci. USSR 1954, 1033.

[5] P. A. DiGiorgio, L. H. Sommer and F. C. Whitmore, J. Am. Chem. Soc. 68, 344 (1946).

[6] P. A. Kantor, J. Am. Chem. Soc. 75, 2712 (1953).

[7] G. F. Tyler, J. Am. Chem. Soc. 77, 770 (1955).

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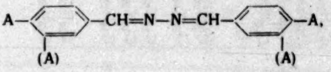
Institute of Organoelement Compounds
of the Academy of Sciences USSR

BENZALAZINE AND ITS DERIVATIVES

I. THE ACTION OF HYDROGEN CHLORIDE ON BENZALAZINE AND ITS DERIVATIVES

B. M. Bogoslovsky and T. I. Yakovenko

Little attention has been paid to the action of hydrogen chloride on benzalazine and its derivatives and to the resultant color changes. When gaseous hydrogen chloride is passed through certain symmetrical derivatives of benzalazine, such as 3,3'-and 4,4'-dihydroxy-, 3,3'-and 4,4'-dimethoxybenzalazines, as well piperonalazine, vanillalazine and 4,4'-bis(dimethylamino-)-benzalazine, dissolved in organic solvents, or on treatment of them with dilute mineral acids, they are known to form deeply colored salts. On the other hand, benzalazine is converted into a hydrochloride whose color is considerably lighter than the color of the starting substance [1-5]. The authors of the previous papers do not suggest structural formulas for the hydrochlorides or attempt to explain this phenomenon. The aim of our investigation was to make a systematic study of benzalazine and of a series of its symmetrical derivatives containing electron-donating and electron-accepting substituents in various positions relative to the central grouping of benzalazine, of the general formula:



$$A-C_6H_3(A)-CH=N-N=CH-C_6H_3(A)-A,$$

where A=H, NO_2, OH, OCH_3, $N(CH_3)_2$, $N(C_2H_5)_2$, Br.

A study was also made of vanillalazine, piperonalazine, 2,2'4,4'-tetrahydroxybenzalazine, 3,3',5,5'-tetrabromobenzalazine and 2,2',4,4',6,6'-hexabromobenzalazine. We prepared three derivatives of benzalazine (4,4'-bisdiethylamino-, 3,3'-dibromo- and 2,2',4,4',6,6'-hexabromobenzalazines) for the first time.

The colors of the various derivatives of benzalazine are fairly similar (see table). A considerable change of color is observed with the hydrochlorides which are obtained by the action of dry hydrogen chloride on solutions of benzalazine derivatives in organic solvents (with the exception of 4,4'-dinitro-, 3,3'5,5'-tetrabromo- and 2,2',4,4',6,6'-hexabromobenzalazines which do not add on hydrogen chloride under our chosen conditions). Depending upon the structure of the benzalazine derivatives, we obtained mono-or dihydrochlorides differing in color from the starting product and exhibiting sensitivity to the action of atmospheric moisture. Results of observations on the change of color during formation of hydrochlorides are presented in the table. Observations were made visually, and also (for some compounds) spectrophotometrically. The reflection curves confirm the visual observations (Figs. 1-5).

Starting compound	Empirical formula	Color of starting compound	Empirical formula of hydrochloride	Color of hydrochloride	Melting point of hydrochloride	
					Found	In literature
Benzalazine	$C_{14}H_{12}N_2$	Yellow	$C_{14}H_{12}N_2 \cdot HCl$	Pale-yellow	148.5°	150 [5]
3,3'-Dinitrobenzalazine	$C_{14}H_{10}O_4N_4$	Yellow	$C_{14}H_{10}O_4N_4 \cdot HCl$	Pale-yellow	185.5-186	
4,4'-Dinitrobenzalazine	$C_{14}H_{10}O_4N_4$	Yellow		Does not add on hydrogen chloride		
3,3'-Bis-(dimethylamino)-benzalazine	$C_{18}H_{22}N_4$	Yellow-orange	$C_{18}H_{22}N_4 .2HCl$	Pale-yellow	186.5-187.5	
4,4'-Bis-(dimethylamino)-benzalazine	$C_{18}H_{22}N_4$	Yellow	$C_{18}H_{22}N_4 \cdot HCl$	Red	244	244 [4]
			$C_{18}H_{22}N_4 \cdot 2HCl$	Yellow	160-163° decomp.	
3,3'-Bis-(diethylamino)-benzalazine	$C_{22}H_{30}N_4$	Yellow	$C_{22}H_{30}N_4 \cdot 2HCl$	Pale-yellow	188-190	
4,4'-Bis-(diethylamino)-benzalazine	$C_{22}H_{30}N_4$	Yellow	$C_{22}H_{30}N_4 \cdot HCl$	Red	188-191 decomp.	
			$C_{22}H_{30}N_4 \cdot 2HCl$	Yellow	195-196	
3,3'- Dihydroxybenzalazine	$C_{14}H_{12}O_2N_2$	Green-yellow	$C_{14}H_{12}O_2N_2 \cdot HCl$	Yellow	174.5-176	
4,4'- Dihydroxybenzalazine	$C_{14}H_{12}O_2N_2$	Yellow	$C_{14}H_{12}O_2N_2 \cdot HCl$	Orange-yellow	240	
3,3'- Dimethoxybenzalazine	$C_{16}H_{16}O_2N_2$	Greenish-Yellow	$C_{16}H_{16}O_2N_2 \cdot 2HCl$	Yellow	130-145	
4.4'- Dimethoxybenzalazine	$C_{16}H_{16}O_2N_2$	Greenish-Yellow-	$C_{16}H_{16}O_2N_2 \cdot HCl$	Yellow	166.5-167	172-177 [2]
Piperonalazine	$C_{16}H_{12}O_2N_4$	Greenish-Yellow	$C_{16}H_{12}O_2N_4 \cdot HCl$	Orange-yellow	205-208	207 [3]
Vanillalazine	$C_{16}H_{16}O_2N_4$	Yellow	$C_{16}H_{16}O_2N_4 \cdot HCl$	Orange-yellow	220-222.5	
2,4,2',4'-Tetrahydroxybenzalazine	$C_{14}H_{12}O_2N_4$	Yellow-green	$C_{14}H_{12}O_2N_4 \cdot HCl$	Yellow-orange	> 360	
3,3'-Dibromobenzalazine	$C_{14}H_{10}N_2Br_2$	Greenish-Yellow	$C_{14}H_{10}N_2Br_2 \cdot 2HCl$	Colorless	159-161	
4,4'-Dibromobenzalazine	$C_{14}H_{10}N_2Br_2$	Light-yellow	$C_{14}H_{10}N_2Br_2 . HCl$	Yellow	221-223	
3,5,3', 5'-Tetrabromobenzalazine	$C_{14}H_8N_2Br_4$	Greenish-Yellow		Does not add on hydrogen chloride		
2,4,6,2',4'6'-Hexabromobenzalazine	$C_{14}H_6N_2Br_6$	Light-yellow		Does not add on hydrogen chloride		

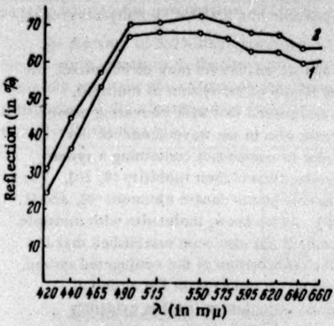


Fig. 1. Reflection curves.
1) Benzalazine; 2) benzalazine monohydrochloride.

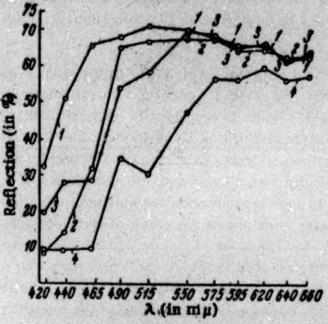


Fig. 2. Reflection curves.
1) 3,3'-dihydroxybenzalazine; 2) 3,3'-dihydroxybenzalazine hydrochloride; 3) 4,4'-dihydroxybenzalazine; 4) 4,4'-dihydroxybenzalazine hydrochloride.

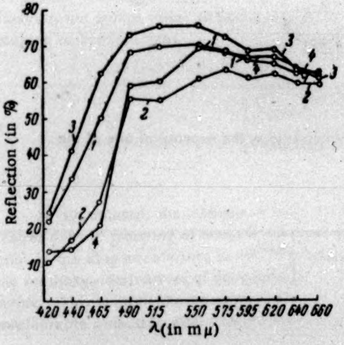


Fig. 3. Reflection curves.
1) 3,3'-dimethoxybenzalazine; 2) 3,3'-dimethoxybenzalazine dihydrochloride; 3) 4,4'-dimethoxybenzalazine; 4) 4,4'-dimethoxybenzalazine hydrochloride.

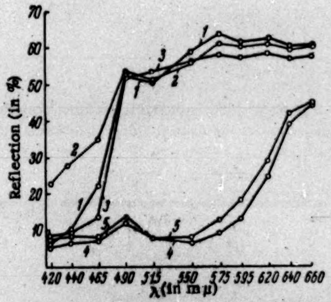
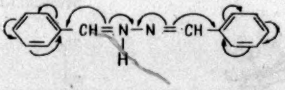


Fig. 4. Reflection curves.
1) 3,3'-bis-(dimethylamino)-benzalazine; 2) 3,3'-bis-(dimethylamino)-benzalazine dihydrochloride; 3) 4,4'-bis-(dimethylamino)-benzalazine; 4) 4,4'-bis-(dimethylamino)-benzalazine monohydrochloride; 5) 4,4'-bis-(dimethylamino)-benzalazine dihydrochloride.

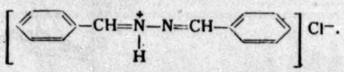
A salt-like character of the compounds is indicated by the spectrophotometric data, since the spectra of the original benzalazines and of their hydrogen chloride-addition products are similar. This hypothesis is in full harmony with the conclusions of V. A. Izmailsky [6,7].

The data in the table indicate that the color of the hydrochlorides of benzaline and its derivatives is directly dependent upon the chemical structure, especially on the nature of the substituents in the benzene rings of benzalazine and their position in relation to the central atomic grouping of benzalazine and in relation to one another. Whereas the color of benzalazine itself and of its meta-derivatives(nitro-, bromo-, dimethylamino- and diethylamino-derivatives) is lightened by addition of hydrogen chloride, and is slightly deepened in the case of meta-hydroxy and meta-methoxy-derivatives, the hydrochlorides of para-derivatives of benzalazine are always more deeply colored than the original benzalazines and the hydrochlorides of the meta-derivatives. The character of the substituents also greatly influences the sharp intensification of color. Particularly interesting in this connection are the methylamino-, diethylamino- and hydroxy-derivatives. A weaker but still appreviable effect is developed by methoxy- and bromo-derivatives. The color is strongly deepened in formation of the hydrochlorides of piperonalazine, vanillalazine and 2,2',4,4'-tetrahydroxybenzalazine.

The following explanation of the color change of benzalazine and its derivatives may be advanced. As we know, the wave-length of absorbed light depends directly upon the length of the system of multiple conjugated bonds in a molecule. Spectrophotometric investigations established that with increasing number of multiple conjugated bonds in the molecule there is a uniform increase also in the wave-length of the absorption maximum [8]. Decisive factors for the development of color in compounds containing a system of multiple conjugated bonds are the number of π-electrons in the molecule and their mobility [8, 10]. The latter in turn depends upon the ability of the atoms in the molecule to accept and donate electrons [9], and it increases when one of the atoms of the molecule acquires a charge [8]. As we know, molecules with multiple conjugated bonds are characterized by a large displacement of electrons; it has also been established that if the charge is able to attach itself to a particular atom entering into the composition of the conjugated system, then this is associated with a lightening of color [9]. From this viewpoint, we can explain the action of hydrogen chloride on benzalazine in the following manner: the color of benzalazine itself is evidently governed by the presence of a system of conjugated double bonds, and the electron density is uniform to a certain degree:



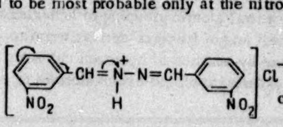
Hydrogen chloride probably leads to formation of an ammonium salt at the expense of one of the nitrogen atoms at the central grouping of benzalazine:



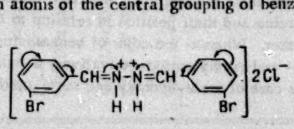
The resultant development of a positive charge at one of the nitrogen atoms entering into the composition of the single system of conjugated double bonds also evidently lightens the color. Since benzalazine is lacking in electron-donating centers, while the mobility of the π-electrons of the benzene ring is relatively slight, the mobility of the π-electrons in this case has little influence on the color.

Similar behavior should be manifested by meta-derivatives of benzalazine independently of the character of the substituent, since the latter, being in the meta-position, does not enter into the system of conjugated double bonds and consequently its unshared and π-electrons do not participate in the conjugation. The foregoing hypothesis is confirmed in great measure by the results of the observations (see table). As already pointed out, the color of 3,3'-dinitro-, 3,3'-dibromo-, 3,3'-bis-(dimethylamino)- and 3,3'-bis-(diethylamino)-benzalazines is lightened by salt formation, while that of 3,3'-dihydroxy- and 3,3'-dimethoxybenzalazines is slightly deepened.

The lightening of color on salt formation in the case of 3,3'-dibromo- and 3,3'-dinitrobenzalazines is evidently caused by the same factors as in the case of benzalazine. Actually, the addition of hydrogen chloride is found to be most probable only at the nitrogen atoms of the central grouping of benzalazine:

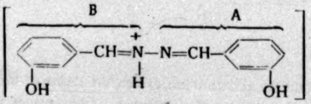


or

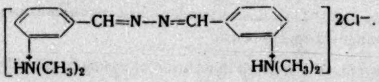


The resultant development of positive charges that upset the system of conjugated double bonds must lead to lightening of the color on formation of hydrochlorides. The unshared and π-electrons of substituents, not participating in the conjugation, evidently cannot exert an influence on the color.

In the case of 3,3'-dihydroxy- and 3,3'-dimethoxybenzalazines, salt formation occurs very probably for the same reason as in the preceding cases, i.e. at the expense of the nitrogen atoms of the central grouping while the resultant observation of deepening of the color must be attributed to the possibility of intramolecular interaction of the electron-donating system (A) with the electron-accepting system (B) in accordance with Izmailsky's theory [11].

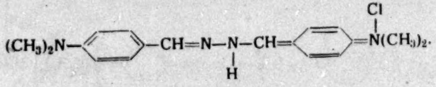


A second molecule of hydrogen chloride, in the case for example of 3,3'-dimethoxybenzalazine, adds on either to the other nitrogen atom of the central grouping of benzalazine or forms an oxonium salt at the expense of one of the methoxyl groups. According to the literature, methoxyl groups in the meta-position can facilitate the formation of oxonium salts [12]. In the case of 3,3'-bis-dimethylamino- and 3,3'-diethylamino- derivatives of benzalazine, which form dihydrochlorides, the color is lighter than in the original compound. We suggest that salt-formation must here take place at the expense of the electron-donating dialkylamino groups which possess a weaker basic character than the nitrogen atoms of the central atomic grouping of benzalazine:



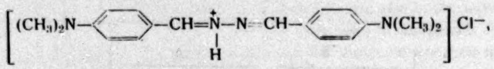
In our opinion, the addition of one of the molecules of hydrogen chloride to a nitrogen atom of the central atomic grouping of benzalazine must be rejected, for in this event we should have deepening of the color of the dihydrochlorides in comparison with the color of the original azine (as in the case of hydroxy- and methoxy- derivatives of benzalazine). Hydrogen chloride does not add on to 3,3'5,5'-tetrabromobenzalazine. This is probably the consequence of the lowering of the basicity of the nitrogen atom due to the considerable inductive effect caused by the accumulation of bromine atoms in the molecule.

In the case of para-derivatives of benzalazine with electron-donating substituents, we should expect deepening of color in salt formation due to intensified shifting of the electronic density due to the presence in the system of conjugated double bonds of substituents carrying unshared or π-electrons in the π-electron system of the molecule, and also due to the stronger intramolecular interaction between the electron-donating and electron-accepting systems. As we see from the data in the table, the color of the hydrochlorides of para-derivatives of benzalazine is indeed deeper than that of the original benzalazines. A particularly strong change of color occurs in the formation of monohydrochlorides of dialkyl derivatives of benzalazine (4,4'-bis-dimethylamino- and 4,4'-bis-diethylaminobenzalazines). We may note that Pesez and Petit [4], who studied the red monohydrochloride of 4,4'-bis-dimethylamino-benzalazine, assigned a quinoid structure to it:



In our opinion, however, a quinoid rearrangement cannot account in this case for the sharp deepening of color (from yellow to red); moreover, the investigations of V. A. Izmailsky [6, 7] indicate the absence of a quinoid grouping in salt formation.

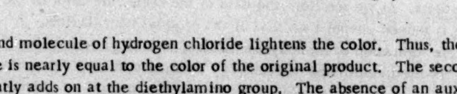
During the action of the first molecule of hydrogen chloride, a proton probably joins on to a nitrogen atom of the central atomic grouping of benzalazine:



since if addition took place at one of the dimethylamino groups the color of the compound would have been more probably lightened due to the exclusion of an auxochrome. This view is supported by the existence of two isomeric forms of salts of aminoazo compounds which differ in color [13]; the color here depends on the place of addition of the elements of hydrogen chloride. Thus, if addition is at a nitrogen atom of the azo group, then the color of the salt is deeper than that of the original azo compound. But if the hydrogen halide combines at the amino or dimethyl amino group, then the color of the salt differs only slightly from that of the original azo product.

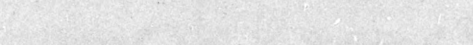
Further support to the view that a molecule of hydrogen chloride first combines at a nitrogen atom of the azomethine group is afforded by the concept of transfer of the reaction center in compounds containing a system of conjugated double bonds, which was put forward by A. N. Nesmeyanov. The latter points out, for example, that in the action of an acidic agent on 4-dimethylaminoazobenzene " ... the attacking hydrogen ion combines not at the expected place of attack (an amino nitrogen) but at the nitrogen which is usually extraordinarily weakly basic" [14], due to transfer of the reaction center of the molecule to another atom along the system of conjugated double bonds.

The positive charge developed as a result of addition of hydrogen chloride to a nitrogen atom of the central atomic grouping of benzalazine also upsets the system of conjugated double bonds, but at the same time it increases the mobility of the π -electrons of the molecule, and the absorption is shifted in the direction of the long waves:



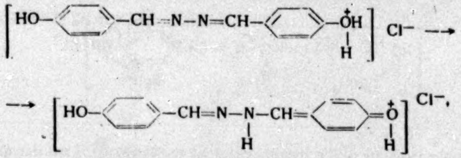
In this case, also, it is possible, just as in the case of meta-derivatives, that an additional factor influencing the color is the intramolecular reaction of the electron-donating system A with the electron-accepting system B.

Addition of a second molecule of hydrogen chloride lightens the color. Thus, the color of 4,4'-bis-diethylaminobenzalazine is nearly equal to the color of the original product. The second molecule of hydrogen chloride evidently adds on at the diethylamino group. The absence of an auxochrome at the same time destroys the electron-donating center, with the result that the color is lightened:



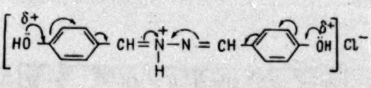
A fairly marked deepening of color on formation of monohydrochlorides is also observed with 4,4'-dihydroxy- and 4,4'-dimethoxybenzalazines, piperonalazine, vanillalazine and 2,2',4,4'-tetrahydroxybenzalazine.

The profound color change in formation of hydrochlorides of 4,4'-dihydroxy- and 4,4'-dimethoxybenzalazines cannot, in our opinion, be explained by the formation of oxonium salts and their further rearrangement to compounds with a quinoid structure, for example:



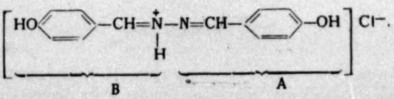
which likewise conflicts with the observations of V. A. Izmailsky, according to whom the quinoid structure cannot account for the color of the salts.

In the cases just considered, hydrogen chloride evidently adds on to a nitrogen atom of the central grouping. The development of a positive charge at the nitrogen atom increases the mobility of the π-electrons of the system, due to which the absorption is displaced towards longer waves, e.g.:

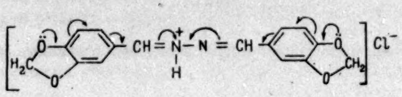


At the same time a partial positive charge is developed at the oxygen atom of the hydroxy or methoxy group due to the shift of the electronic density, and this hinders the addition of the second molecule of hydrogen chloride. In consequence the derivatives of azines in question, only give monohydrochlorides.

Intramolecular reaction between the electron-donating system (A) and the electron-accepting system (B) is also a possibility in the above cases, according to the scheme:

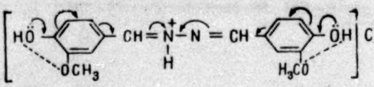


Since the color of the hydrochlorides of vanillalazine and piperonalazine is nearly the same as that of 4,4'-dihydroxybenzalazine hydrochloride, we can advance the same explanation, namely the formation of an ammonium salt at the expense of one of the nitrogen atoms of the central atomic grouping. The bond between the oxygen in piperonalazine and the methylene group evidently exerts little influence upon the change of electronic structure of the compound as a whole.



Vanillalazine hydrochloride very probably possesses a similar electronic structure. In this case again, the addition of a molecule of hydrogen chloride is only possible at the expense of a nitrogen atom. But the formation of an oxonium salt is improbable since the hydroxy and methoxy groups in the ortho-position are connected by an intramolecular hydrogen bond, as was proved by the investigations of M. I. Batuev on guaiacol [15].

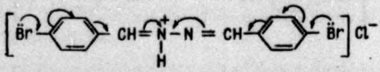
The presence of an intramolecular hydrogen bond, however, does not substantially prevent the π-electrons of the hydroxy group from participating also in the π-conjugation:



The described electronic structure of the hydrochloride of vanillalazine is similar to that of the hydrochlorides of 4,4'-dihydroxybenzalazine and piperonalazine and may account for their substantially identical color.

No full explanation can yet be given of the rather lighter color of the monohydrochloride of 2,2',4,4'-tetrahydroxybenzalazine in comparison with the color of the hydrochloride of 4,4'-dihydroxybenzalazine.

In the case of 4,4'-dibromobenzalazine, whose bromine atoms manifest relatively weak electron-donating properties, the formation of the monohydrochloride leads to only slight deepening of color. Addition of hydrogen chloride evidently likewise takes place at the expense of a nitrogen atom of the central grouping:



4,4'-Dinitro- and 2,2',4,4',6,6'-hexabromobenzalazines do not add on hydrogen chloride. The probable cause of this behavior is the considerable migration of the electron-donating center from the nitrogen atoms of the azine grouping, due in the case of 4,4'-dinitrobenzalazine to the presence of electron-accepting substituents, and in the case of 2,2',4,4',6,6'-hexabromobenzalazine to the great inductive effect of the large number of bromine atoms.

EXPERIMENTAL

Preparation of benzaline and its derivatives. Benzalazine and its derivatives were prepared by reaction of an aqueous alcoholic solution of 2 moles of the appropriate aldehyde with hydrazine while heating on a boiling water bath for 1-2 hours. The products usually came down and after numerous recrystallizations they were subjected to further study. 3,3'-Dibromo-, 2,2',4,4'6,6'-hexabromo-and 4,4'-bis-diethylaminobenzalazines, not previously described in the literature, were obtained by the above method and had the following properties: 3,3'-Dibromobenzalazine: greenish-yellow needles; readily soluble in acetone, alcohol and ether. M. p. 160-161°.

Found %: N 7.65. $C_{14}H_{10}N_2Br_2$. Calculated %: N 7.73.

2,2',4,4',6,6'-Hexabromobenzalazine: light-yellow needles from chloroform; good solubility in alcohol and benzene. M. P. 238.5-239.5°.

Found %: N 4.4. $C_{14}H_6N_2Br_6$. Calculated %: N 4.35.

4,4'-Bis-diethylaminobenzalazine: yellow crystals from benzene; good solubility in alcohol, poor solubility in ether and ligroine. M. p. 184-185°.

Found %: N 16.09. $C_{22}H_{30}N_4$. Calculated %: N 16.20.

Preparation of hydrochlorides of benzalazine and its derivatives. Benzalazine (or a derivative) was dissolved in the cold in one of the dehydrated organic solvents (benzene, ether, chloroform or acetone), after which a stream of dry hydrogen chloride was passed into the solution for 15-20 minutes. The precipitated hydrochloride was collected, washed with absolute ether and dried to constant weight in vacuum. A weighed sample of the hydrochloride was dissolved in a little aqueous alcohol and analyzed for its chlorine content either by direct titration with 0.1 N KOH or by the Volhard method (in the case of hydroxy derivatives of benzalazine). Results are given in the table.

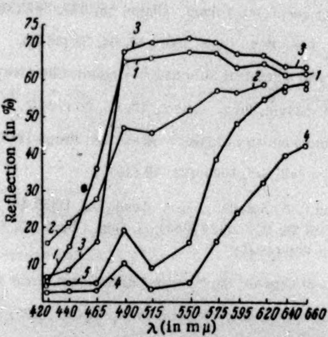


Fig. 5. Reflection curves. 1) 3,3'-bis-(diethylamino)-benzalazine, 2) 3,3'-bis-(diethylamino)-benzalazine dihydrochloride, 3) 4,4'-bis-(diethylamino)-benzalazine, 4) 4,4'-bis-(diethylamino)-benzalazine monohydrochloride, 5) 4,4'-bis-(diethylamino)-benzalazine dihydrochloride.

SUMMARY

1. The preparation was carried out of 18 symmetrical derivatives of benzalazine containing various substituents of an electron-donating and electron-accepting character in different positions in relation to the central grouping of benzalazine.

2. On treatment with dry hydrogen chloride, most of the synthesized derivatives form hydrochlorides which differ markedly in color and a number of other properties from the starting compounds.

3. Analysis of the hydrochlorides shows that benzalazine and its derivatives can add on one or two molecules of hydrogen chloride depending upon their chemical structure. The majority of the hydrochlorides that were prepared and investigated have not been described in the literature.

4. The color of the hydrochlorides of benzalazine derivatives depends directly upon the chemical structure of the compound, in particular upon the nature of the substituents and their position relative to the central atomic grouping of benzalazine and probably to one another.

5. On the basis of modern electronic theory an attempt is made to explain the changes of color of benzalazine derivatives observed after treatment with dry hydrogen chloride.

6. The following have been prepared and studied for the first time: 3,3'-dibromo-, 2,2',4,4',6,6'-hexabromo- and 4,4'-bis-(diethylamino)-benzalazines; also the hydrochlorides of 3,3'-dinitro-, 3,3'-bis- (dimethylamino)-, 4,4'-bis(dimethylamino)-, 3,3'-bis-(diethylamino)-, 4,4'-bis-(diethylamino)-, 3,3'-dihydroxy-, 4,4'-dihydroxy-, 3,3'-dimethoxy-, 2,2',4,4'-tetrahydroxy-, 3,3'-dimethoxy-, 4,4'-dimethoxy-, 3,3'-dibromo- and 4,4'-dibromobenzalazines.

LITERATURE CITED

[1] E. Noelting, Ann. Chim. (8), 19, 514 (1910).

[2] S. Shoesmith and E. Slater, J. Chem. Soc. 127, 1490 (1925).

[3] T. Curtius, J. Prog. Chem. 85,424, 458 (1912).

[4] M. Pesez and A. Petit, Bull. Soc. Chim., 1947, 122; L. Andrieth and B. Ackerson, The Chemistry of Hydrazine (New York, 1951),164.

[5] T. Curtius and E. Quedenfeldt, J. Prog. Chem. 58, 373, 391 (1898).

[6] V. A. Izmailsky, J. Russ. Phys. Chem. Soc. 47, 64, 73 (1915).

[7] State of the Theory of Chemical Structure in Organic Chemistry*(Acad. Sci. Press, 1952), 146.

[8] G. N. Lewis and M. Calvin, Prog. Chem., 10, 45, 66 (1941).

[9] A. N. Terenin, Photochemistry of Dyes*(Acad. Sci. Press, 1947), 49, 51.

[10] F. S. Shifrin, Proc. Acad. Sci. USSR (29, 28 (1940).

[11] V. A. Izmailsky and P. A. Solodkov, Proc. Acad. Sci. USSR 60, 587 (1948); 75, 391 (1950); V. A. Izmailsky, Proc. Acad. Sci. USSR 26, 906, 912 (1940); J. Gen. Chem. 13, 685 (1943); V. A. Izmailsky, A. V. Belochvetov, J. Gen. Chem. 11, 650 (1941).

[12] I. Houben, Methods of Organic Chemistry* (State Chem. Press 1935), Vol. 3 part 3, 143.

[13] P. Pfeifer, Organische Molekulverbindungen (Stuttgart, 1927) 197.

[14] A. N. Nesmeyanov, Sci. Mem. Moscow State Univ., No. 132, part 7, 7 (1950).

[15] M. I. Batuev, Proc. Acad. Sci. USSR 47, 100 (1945).

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Moscow Institute of Textiles

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THE REACTION OF DIALKYLPHOSPHOROUS ACIDS WITH ALDEHYDES AND KETONES

ESTERS OF α-HYDROXY-NITROBENZYLPHOSPHINIC ACIDS

V. S. Abramov

In 1950 I discovered the reaction of condensation of dialkylphosphorous acids with aldehydes and ketones [1] which leads to formation of esters of substituted α-hydroxymethylphosphinic acid. We made a systematic study of these compounds [2]. Apart from the work published, we also studied the action of dialkylphosphorous acids on various compounds containing a carbonyl group, such as esters and amides of carboxylic acids. The susceptibility of carbonyl compounds to enter into reaction with nucleophilic reactants decreases in the following order: aldehydes > ketones > esters > acids. Acid amides manifest the same effect as esters [3]. Although the reactivity also falls off in the same order, it was nevertheless tempting to investigate the reaction of dialkylphosphorous acids with esters, in particular of formic acid. The latter have an aldehydic group bound to an alkoxy group. We studied the action of dialkylphosphorous acids on methyl and ethyl formates and on methyl and ethyl benzoates. The reactions do not go under the usual conditions that we have described for aldehydes and ketones in presence of alkoxides of the alkali metals. Negative results were likewise obtained in reactions with other compounds containing a carbonyl group.

Other investigators have also studied the condensation of dialkyl phosphorous acids with carbonyl compounds. An American patent [4] describes the condensation of diethyl phosphrous acid with aldehydes and ketones using triethylamine as catalyst. Chloral and dialkyl phosphorous acids react in the entire absence of a catalyst [5]. The reaction is exothermic, so that the products of reaction must be cooled with water.

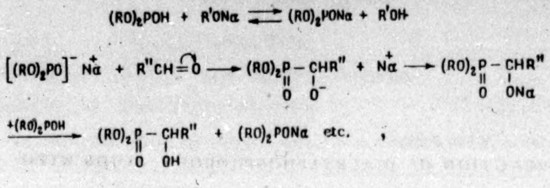
In a review article [6] A. N. Pudovik describes methods of preparation of esters of alkyl phosphinic acids, including esters of α-hydroxyalkyl phosphinic acids. No reference is made in the paper, however, to the work of V. Abramov [1] and A. N. Pudovik [7], possibly in order that the review of the condensations of dialkyl phosphorous acids with aldehydes should commence with his own work [8].

The present work deals with condensations of dialkyl phosphorous acids with nitrobenzaldehydes. Addition of a catalyst (a solution of sodium ethoxide in methyl alcohol) causes the color of the reaction mass to change from green to blue. Heat evolution is not observed when dialkyl phosphorous acids are mixed with nitrobenzaldehydes. Prolonged standing of the reaction mixture at room temperature or better, at a slightly elevated temperature (30-50°), leads, however, to formation of esters of α-hydroxynitrobenzylphosphinic acid. The esters gradually crystallize from the liquid mixture of reactants. Condensation of dialkyl phosphorous acids with nitrobenzaldehydes can be accelerated by using metallic sodium diethyl phosphite as catalyst. The reaction then goes in the course of a few days.

The rate of the above condensations is very much slower than that of others so that we cannot draw any conclusions about the effect of the nitro group on the reaction course.

Properties and yields of esters of α-hydroxynitrobenzylphosphinic acids are presented in Tables 1 and 2.

When using sodium ethoxide as catalyst, the condensations of dialkyl phosphorous acids with aldehydes and ketones proceed in alcoholic solution with remarkably high speed with much evolution of heat. They may be represented by the scheme:



$$(RO)_2POH + R'ONa \rightleftharpoons (RO)_2PONa + R'OH$$

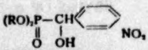
$$[(RO)_2PO]^- \overset{+}{Na} + R''CH{=}O \longrightarrow (RO)_2\underset{\substack{\| \\ O}}{P}-\underset{\substack{| \\ O^-}}{C}HR'' + \overset{+}{Na} \longrightarrow (RO)_2\underset{\substack{\| \\ O}}{P}-\underset{\substack{| \\ ONa}}{C}HR''$$

$$\xrightarrow{+(RO)_2POH} (RO)_2\underset{\substack{\| \\ O}}{P}-\underset{\substack{| \\ OH}}{C}HR'' + (RO)_2PONa \text{ etc. },$$

i. e., an ionic mechanism is involved.

TABLE 1

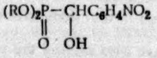
Esters of α-Hydroxy-m-nitrobenzylphosphinic Acid



R	Melting point	Yield of recrystallized substance (%)	Phosphorus content (%)	
			Found	Calculated
CH_3	86—87°	31.8	11.55, 11.72	11.88
C_2H_5 . . .	92—93	62.8	10.52, 10.65	10.73
C_3H_7 . . .	68—69	49.5	9.59, 9.75	9.78
iso-C_3H_7 .	101—102	73.0	9.83, 9.84	9.78
C_4H_9 . . .	40—42	63.0	8.87, 8.93	8.98
iso -C_4H_9 . .	80—81	48.9	8.92, 9.03	8.98

TABLE 2

Esters of α-Hydroxy-nitrobenzylphosphinic Acid



$$(RO)_2\underset{\substack{\| \\ O}}{P}-\underset{\substack{| \\ OH}}{C}HC_6H_4NO_2$$

R	Position of NO_2 group	Melting point	%Yield of recrystallized substance	Phosphorus content (%)	
				Found	Calculated
CH_3	Ortho	109—109.5°	53.2	12.06, 12.17	11.88
iso -C_3H_7 .	Ortho	116	63.5	9.57, 9.67	9.78
CH_3	Para	131—132	50.8	11.85, 11.74	11.88

Condensations of dialkyl phosphorous acids with nitrobenzaldehydes without catalyst and in presence of metallic sodium diethyl phosphite take place without release of heat and are completed after a long period. It must be assumed that they proceed by a different mechanism, i. e., by a molecular mechanism as is usually the case for organic reactions, or possibly by an ionic-molecular mechanism. Other reactions proceed similarly in analogous conditions. On introducing metallic sodium into a mixture of the benzaldehyde and diethyl phosphorous acid, no heat is evolved and the reaction goes quietly. It is completed in 3 days with formation of a dense crystalline mass. Cyclohexanone and diethyl phosphorous acid give a crystalline product only after brief heating and standing for a week. Yield about 50%. Both these reactions go very vigorously with much heat development in presence of an alcoholic solution of sodium ethoxide [2]. After cooling, a dense crystalline mass is obtained. The alcoholic medium promotes ionization.

The methyl esters of α-hydroxynitrobenzylphosphinic acids exhibit slight physiological activity.

EXPERIMENTAL

Dialkyl phosphorous acids were reacted with nitrobenzaldehydes in small flasks into which equimolar amounts of acid and aldehyde were charged. The contents of the flask were cautiously heated until the nitrobenzaldehyde had completely dissolved. The nitrobenzaldehyde crystallized out when the solution was kept at room temperature. Reaction mixtures are best kept at temperatures of 30-50°. The reaction products then remain in solution. Crystals of esters began to appear after a very considerable period of one to two months. The reaction was considered at an end when the content of the flask, or a considerable proportion, was transformed into a dense crystalline mass. The crystals were filtered, washed with cyclohexane and recrystallized from cyclohexane or from cyclohexane-alcohol or aqueous alcohol.

Experiments were repeated with introduction into the reaction mixture of a small piece (size of a small pea) of metallic sodium or two to three drops of sodium diethyl phosphite. The sodium diethyl phosphite was prepared by the action of metallic sodium on diethyl phosphorous acid in a test tube. It formed a viscous mass. The reaction was completed more quickly in presence of a catalyst — in a few days to two weeks.

SUMMARY

Nitrobenzaldehydes react with dialkyl phosphorous acids without a catalyst and give esters of α-hydroxynitrobenzylphosphinic acids. The reaction is slow at 30-50°. The condensations can be accelerated by using metallic sodium or sodium diethyl phosphite as catalyst.

9 esters of α-hydroxynitrobenzylphosphinic acids were prepared.

LITERATURE CITED

[1] V. S. Abramov, Proc. Acad. Sci. USSR 73, 487 (1950).

[2] V. S. Abramov, J. Gen. Chem. 22, 647 (1952) (T. p. 709) *; V. S. Abramov, and L. G. Semenova, Proc. Acad. Sci. USSR 84, 281 (1952); V. S. Abramov, R. V. Dmitrieva and A. S. Kapustina, J. Gen. Chem. 23, 257 (1953) (T. p. 269)*; V. S. Abramov, Yu. A. Bochkova and A. D. Polyakova, J. Gen. Chem. 23, 1013 (1953) (T. p. 1061)*; V. S. Abramov and L. P. Semenova, J. Gen. Chem. Suppl. Vol. I, 393 (1953); V. S. Abramov and N. S. Kuznetsov, J. Gen. Chem. Suppl. Vol. I, 398 (1953); V. S. Abramov and N. A. Ilyina, J. Gen. Chem. 24, 124 (1954) (T. p. 121) *; V. S. Abramov and A. S. Nazmutdinova, J. Gen. Chem. 25, 1141 (1955) (T. p. 1095)*.

[3] A. Remik, Electronic Concepts in Organic Chemistry (1950), 147.**

[4] U. S. Patent 2579810 (1951); C. A. 1952, 6140.

[5] W. F. Barthel, P. A. Giang and S. A. Hall, J. Am. Chem. Soc. 76, 4186 (1954).

[6] A. N. Pudovik, Prog. Chem. 23, 547 (1954).

[7] A. N. Pudovik, Proc. Acad. Sci. USSR 73, 499 (1950).

[8] A. N. Pudovik and Yu. P. Kitaev, J. Gen. Chem. 22, 467 (1952) (T. p. 531)*

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* T. p. = C. B. Translation pagination.

** In Russian.

THE REACTION OF DIALKYL PHOSPHOROUS ACIDS WITH ALDEHYDES AND KETONES

XI. ESTERS OF α-HYDROXY-p-METHYLBENZYLPHOSPHINIC ACID

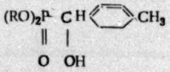
V. S. Abramov and Sh. Pall

This paper reports experiments on the condensation of p-tolualdehyde with dialkyl phosphorous acids. The condensation was performed by dropwise addition of a solution of sodium methoxide in methyl alcohol to an equimolar mixture of p-tolualdehyde and dialkyl phosphorous acid. The reaction went rapidly and with much heat development. The reaction velocity was approximately the same as that of condensations of dialkyl phosphorous acids with benzaldehyde. It was not possible to establish any differences between these reactions. It must be assumed that the reactions proceed by an ionic mechanism [1].

The properties of the prepared esters of α-hydroxy-p-methylbenzyl-phosphinic acid are presented in the table.

TABLE

Esters of α-Hydroxy-p-methylbenzylphosphinic Acid



$(RO)_2P(=O)-CH(OH)-C_6H_4-CH_3$

Temperature rose during reaction from 20° to		Melting point of ester	Phosphorus content		Yield (in %)
			Found	Calculated	
95°	CH_3	92—93°	13.43, 13.45	13.48	84
78	C_2H_5	95—96	11.99, 11.93	12.02	50
94	n -C_3H_7	45—52	10.82, 10.65	10.84	58
101	iso -C_3H_7	124—125	10.74, 10.73	10.84	70
86	C_4H_9	—	9.86, 9.80	9.87	91
48	iso -C_4H_9	67—68	9.84, 9.78	9.87	25

The esters are sparingly soluble in cyclohexane, readily soluble in alcohol. Methyl, ethyl and isopropyl esters of α-hydroxy-p-methyl-benzylphosphinic acid crystallize nicely. The propyl and isobutyl esters do not crystallize satisfactorily. These esters are camphor-like in properties. The propyl ester could not be recrystallized and therefore has an unsharp melting point.

The butyl ester of α-hydroxy-p-methylbenzylphosphinic acid is a viscous, glycerol-like liquid (purified by washing [2]):

$$n_D^{20}\ 1.4950,\ d_4^{20}\ 1.1248,\ MR_D\ 81.41.\ C_{16}H_{27}O_4P.\ \text{Calc. } 79.85.$$

SUMMARY

Six esters of α-hydroxy-p-methylbenzylphosphinic acid were prepared.

LITERATURE CITED

[1] V. S. Abramov, Proc. Acad. Sci. USSR 73, 487 (1950).

[2] V. S. Abramov and A. S. Nazmutdinova, J. Gen. Chem. 25, 1141 (1955) (T. p. 1095) •

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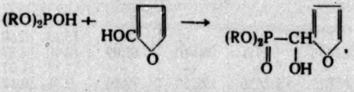
REACTIONS OF DIALKYLPHOSPHOROUS ACIDS WITH ALDEHYDES AND KETONES

XII. ESTERS OF α-HYDROXY-α-FURYLPHOSPHINIC AND α-HYDROXY-α-THENYLPHOSPHINIC ACIDS

V. S. Abramov and A. S. Kapustina

We previously published a communication on the reaction of dialkylphosphorous acids with 6-quinolinealdehyde. The products of this reaction were esters of α-hydroxy-(6-quinolyl)-methylphosphinic acid, i. e., esters of substituted α-hydroxymethylphosphinic acid containing an heterocyclic radical were obtained [1]. It was interesting to perform the condensation of dialkylphosphorous acids with other heterocyclic aldehydes. In the present paper we describe the results of reaction of dialkylphosphorous acids with furfural and α-thiophenealdehyde. The two latter substances can react with dialkylphosphorous acids either at the carbonyl group [2] or at the double carbon-carbon bond [3], and possibly also at the conjugated system of double bonds. The investigation showed that under our chosen conditions the reactions go at the carbon-oxygen bond and give esters of α-hydroxyfurylphosphinic and α-hydroxy-α-thenylphosphinic acids according to the scheme:



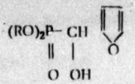
where sulfur replaces oxygen in the ring in the case of thiophenealdehyde.

A catalyst was added to an equimolar mixture of dialkylphosphorous acid and furfural or α-thiophenealdehyde. For the catalyst we used a solution of sodium methoxide in methyl alcohol, triethylamine (mentioned in an American patent [4]), and pyridine. It must be pointed out that reactions with furfural and α-thiophenealdehyde go less energetically than with aliphatic or aromatic aldehydes. Triethylamine is a weaker catalyst than solutions of alkoxides of alkali metals and it must be used in larger amount. The temperature of the reaction mixture rises slowly and gradually. In some cases, however, triethylamine is a more acceptable and convenient catalyst. The reactions go very slowly with pyridine; actually it is difficult to establish whether pyridine functions as a catalyst.

Properties and yields of the prepared esters of α-hydroxy-α-furylphosphinic acid and α-hydroxy-α-thenylphosphinic acid are presented in Tables 1 and 2.

TABLE 1

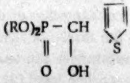
Esters of α-Hydroxy-α-furylphosphinic Acid



R	n_D^{20}	d_4^{20}	MR_D		Phosphorus content (%)		Yield (%)
			Found	Calculated	Found	Calculated	
CH_3	—	—	—	—	14.98, 14.85	15.04	33
C_2H_5	1.4760	1.2155	54.32	54.66	13.20, 13.25[*]	13.25	60
	1.4795	1.2202	54.42		13.07, 12.94		50
iso-C_3H_7	—	—	—	—	11.62, 11.66	11.83	47
C_4H_9	1.4700	1.1044	73.26	73.13	10.47, 10.45	10.69	44
iso-C_4H_9	1.4655	1.0945	73.33	73.14	10.10, 10.51	10.69	44

TABLE 2

Esters of α-Hydroxy-α-thenylphosphinic Acid



R	n_D^{20}	d_4^{20}	MR_D		Phosphorus content (%)		Yield (%)
			Found	Calculated	Found	Calculated	
CH_3	—	—	—	—	13.73, 13.60	13.96	35
C_2H_5	1.5135	1.2451	60.40	61.09	12.40, 12.39	12.40	53
iso-C_3H_7	—	—	—	—	11.14, 11.07	11.15	31
C_4H_9	1.5015	1.1436	79.53	79.56	9.95, 10.12	10.13	67
iso-C_4H_9	1.4960	1.1340	79.83	79.56	10.18, 10.06	10.13	54
C_3H_5	1.5280	1.2321	69.48	69.39	11.30, 11.31	11.31	61

EXPERIMENTAL

Methyl ester of α-hydroxy-α-furylphosphinic acid. Triethylamine was run into a mixture of 19.2 g furfural and 22.0 g dimethylphosphorous acid. The temperature of the reaction mixture started to rise only after 5-6 drops of triethylamine had been added, and it rose to 95°. The mixture was cooled with a water stream. The reaction product turned yellow and thickened up considerably before crystallizing. It was recrystallized from a mixture of anhydrous alcohol and cyclohexane (20:80). Yield 13.5 g (32.8 %). M. p. 47-48°. A determination of the hydroxyl group gave 8.50% (calculated 8.25%).

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[*] B. p. 179-180° at 3 mm with very slight decomposition.

Ethyl ester of α-hydroxy-α-furylphosphinic acid. A few drops of sodium methoxide solution were added to a mixture of 19.2 g furfural and 27.6 g diethylphosphorous acid. The reaction mixture turned brown and the temperature rose to 86°. Purification was effected by washing with an equal volume of sodium bisulfite solution and with sodium chloride solution, since the product was appreciably soluble in water. The reaction goes more slowly with triethylamine and the product is light-yellow. A colorless product is obtained if the reaction is conducted at a temperature not higher than 45°. Yield 24.0 g (50 %). In one of the experiments the reaction product was distilled in vacuum and had b. p. 179-180° at 3 mm. Very slight decomposition occurred during distillation. Table 1 shows that in the case of the distilled product the constants were slightly lower and the phosphorus content was higher, evidently due to the presence of decomposition products.

Isopropyl ester of α-hydroxy-α-furylphosphinic acid. To a mixture of 12.1 g furfural and 21.0 g diisopropylphosphorous acid was added 3 drops of sodium methoxide solution. The temperature rose to 38°. After a period of 12 hours, another few drops of sodium methoxide were added. The temperature rose to 70°. The product turned pale-yellow and thickened considerably; after a short time it crystallized. The substance was twice recrystallized from a mixture of alcohol and cyclohexane (20:80) M. p. 61-62°. Yield 15.2 g (47 %).

Butyl ester of α-hydroxy-α-furylphosphinic acid. 2 ml triethylamine was gradually added to a mixture of 19.2 g furfural and 38.8 g dibutylphosphorous acid. No considerable rise of temperature was observed. The progress of the reaction was followed through the change in refractive index which became constant after 72 hours. The product was purified by washing with sodium bisulfite solution and sodium chloride solution. It was dried and decolorized by passing through a column packed with anhydrous alumina, 20 cm. high. Yield 25.5 g (44 %, large losses in the column).

Isobutyl ester of α-hydroxy-α-furylphosphinic acid. 0.1 ml triethylamine was added to a mixture of 9.6 g furfural and 19.4 g diisobutylphosphorous acid. No temperature rise was observed. The course of the reaction was followed from the change in refractive index. The reaction was completed in 60 hours. The product was purified by washing with sodium bisulfite solution and sodium chloride solution, and dried to constant weight and constant refractive index in a vacuum-desiccator. Yield 12.8 g (44 %).

Methyl ester of α-hydroxy-α-thenylphosphinic acid. Several drops of a solution of sodium methoxide were run into a mixture of 40 g α-thiophenealdehyde and 3.9 g dimethylsphosphorous acid. The temperature of the reaction mixture rose rapidly to 82°. The product crystallized when it was poured off. Recrystallization was effected from a mixture of alcohol and cyclohexane (20:80). M. p. 65-66°. Yield 2.9 g (36 %). A determination of the hydroxyl group gave a value of 7.94 and 7.74% (calculated 7.65%).

Ethyl ester of α-hydroxy-α- thenylphosphinic acid. A total of 2ml triethylamine was run gradually into a mixture of 13.5 g α-thiophenealdehyde and 16.7 g diethylphosphorous acid. The temperature of the reaction mass gradually rose to 100°. The product was purified by washing with a solution of sodium bisulfite and sodium chloride. Yield 16.0 g (53 %). Determination of the hydroxyl group gave 6.96 and 6.82% (calculated 6.80%).

Isopropyl ester of α-hydroxy-α-thenylphosphinic acid. To a mixture of 5 g α-thiophenealdehyde and 7.4 g diisopropylphosphorous acid was added a few drops of triethylamine. The temperature of the reaction mixture rose to 80° and on cooling the product crystallized completely. After two recrystallizations the product had m. p. 71-72° Yield 3.8 g (31 %).

Butyl ester of α-hydroxy-α-thenylphosphinic acid. 0.3 ml triethylamine was run into a mixture of 4.0 g α-thiophenealdehyde and 6.9 g dibutylphosphorous acid. The temperature of the reaction mixture rose to 80° and the product became very viscous. Purification was effected by washing with a solution of sodium bisulfite and sodium chloride. The product was dried in a vacuum-desiccator. Yield 7.3 g (67 %).

Isobutyl ester of α-hydroxy-α-thenylphosphinic acid was prepared as described above. The temperature of the reaction mass rose to 84°. Yield 5.9 g (54 %).

Allyl ester of α-hydroxy-α-thenylphosphinic acid. Into a mixture of 2.9 g α-thiophenealdehyde and 4.2g diallylphosphorous acid was run 0.1 ml triethylamine. No marked rise in temperature of the reaction mass was observed. The product was purified by washing with a solution of sodium bisulfite and common salt, and was dried in a vacuum-desiccator. Yield 4.3 g (61%).

SUMMARY

1. In presence of sodium methoxide and triethylamine, furfural and α-thiophenealdehyde react with dialkylphosphorous acids; addition of the latter takes place at the carbonyl group.

2. Five esters of α-hydroxy-α-furylphosphinic acid and six esters of α-hydroxy-α-thenylphosphinic acid were prepared.

LITERATURE CITED

[1] V. S. Abramov and A. S. Kapustina, J. Gen. Chem. 24, 311 (1954) (T. p. 313) *

[2] V. S. Abramov, Proc. Acad. Sci. USSR 73, 487 (1950).

[3] B. A. Arbuzov and A. N. Pudovik, Proc. Acad. Sci. USSR 73, (1950).

[4] U. S. Patent 2579810 (1951).

[5] V. S. Abramov and A. S. Nazmutdinova, J. Gen. Chem. 25, 1141 (1955) (T. p. 1095)*

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TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

X. SILICOANHYDRIDES OF MONOBASIC SATURATED ORGANIC ACIDS IN THE SYNTHESIS OF ALKYL β-CHLOROVINYL KETONES

Yu. K. Yuryev and G. B. Elyakov

The most convenient method for the preparation of alkyl β-chlorovinyl ketones with facility and in good yields is the addition of acid chlorides to acetylene in presence of anhydrous aluminum chloride. A. N. Nesmeyanov, N. K. Kochetkov and M. I. Rybinskaya [1] have thoroughly developed this method and have demonstrated the possibility of using chlorides of various acids in this reaction, thereby proving that the reaction has a general character. The extremely reactive alkyl β-chlorovinyl ketones are convenient starting substances for the synthesis of compounds of other classes and in particular of various heterocyclic systems [2].

In our previous publications we showed the possibility of wide preparative application of tetraacyloxysilanes (mixed anhydrides of organic and orthosilicic acids) to acylations of the thiophene [3], selenophene [4] and pyrrole [5] rings, as well as to condensations with aromatic aldehydes leading to α, β-unsaturated acids [6]. Having established that in these reactions silicoanhydrides of organic acids behave like acid anhydrides, we obtained numerous examples not only of the possibility but also of the advantages of using tetraacyloxysilanes in these reactions in place of anhydrides and acid chlorides. Tetraacyloxysilanes are easily and simply obtained in a suitable solvent in which the reaction is also usually carried out without their previous isolation in the pure form.

Up to now the reaction of silicoanhydrides of monobasic saturated organic acids with acetylene has not been studied. Apart from this, it was of interest to examine the possibility of using this reaction for the synthesis of alkyl β-chlorovinyl ketones; another objective was to establish whether tetraacyloxysilanes react directly or whether the reactants are acid chlorides that might be formed from them by the action of anhydrous aluminum chloride or anhydrous tin chloride.

In the present work we reacted acetylene in presence of anhydrous aluminum chloride with the silicoanhydrides of acetic, propionic, n-butyric and n-caproic acids and obtained the corresponding alkyl β-chlorovinyl ketones in yields of 30-41% reckoned on the acid brought into reaction. These yields are lower than those obtained when using acid chlorides in the reactions, although in some cases the difference in yields is small (for example for ethyl β-chlorovinyl ketone). If acetylene had reacted not with the silicoanhydride itself but with the acid chloride, which latter might have been formed from the former under the action of aluminum chloride, then the introduction of hydrogen chloride into the reaction medium should undoubtedly promote this process and lead to a higher yield of alkyl β-chlorovinyl ketone. Passage of hydrogen chloride, however, into the reaction mass in one of the experiments on preparation of methyl β-chlorovinyl ketone did not increase the yield of chlorovinyl ketone.

Another interesting feature of the reaction, here described, of silicoanhydrides of saturated monobasic organic acids with acetylene is its fundamental difference from the reactions of silicoanhydrides that we have studied in the past. In contrast to former reactions of tetraacyloxysilanes, their reaction with acetylene in presence of aluminum chloride is an addition reaction. Addition of silicoanhydrides of saturated monobasic organic acids, such as silicoacetic anhydride, to acetylene must lead to formation of an ester of orthosilicic acid and alkyl β-hydroxyvinyl ketone

$$Si\,(OCOCH_3)_4 + 4CH \equiv CH \xrightarrow{AlCl_3} [Si(OCH = CH-COCH_3)_4],$$

which under the action of aluminum chloride undergoes cleavage with formation of methyl β-chlorovinyl ketone and a haloaluminum salt of orthosilicic acid:

$$[Si(OCH{=}CH{-}CO{-}CH_3)_4] + 4AlCl_3 \rightarrow 4CH_3COCH{=}CHCl + Si(OAlCl_2)_4.$$

We therefore suggest that a reaction of the Kondakov type [7] is involved when silicoanhydrides of saturated organic acids enter into reaction with acetylene in presence of anhydrous aluminum chloride, i. e., the reaction goes directly, and the formation of alkyl β-chlorovinyl ketones in this case is the result of cleavage by aluminum chloride of the initially formed products of addition — esters of orthosilicic acid and alkylhydroxyvinyl ketones.

Cleavage of esters by aluminum chloride with formation of acid salt and halogen derivative has been described by Hartmann and Gattermann [8], and there is no doubt that an ester of orthosilicic acid and alkyl-β-hydroxyvinyl ketone must be easily susceptible to such a cleavage.

EXPERIMENTAL

Experimental procedure. 100 ml anhydrous carbon tetrachloride, 0.3 mole organic monobasic acid and 0.075 mole silicon tetrachloride were charged into a three-necked flask (250 ml) fitted with stirrer, reflux condenser with calcium chloride tube, thermometer and tube for introduction of acetylene. Heating was effected on a water bath at first at 60-70° and later on the boiling bath until hydrogen chloride ceased to come off; cooling was then effected with iced water and the first portion of pulverized aluminum chloride was added; at the same time a stream of dry acetylene was passed through, at first weakly and then more intensively. Aluminum chloride (0.45 mole in all) was introduced in small portions in the course of 2-2½ hours; acetylene was passed in for 4 for 6 hours depending upon the ketone being prepared (see below), while the temperature of the reaction mixture was maintained at 5-10°. The reaction mass, usually colored brown towards the end of the reaction, was decomposed by pouring on to 300-500 g of ice, transferred to a large round-bottomed flask and distilled with steam at a pressure of 170-180 mm mercury. The distillate was extracted with ether, and the ether extracts were washed with 10 % sodium carbonate and with water and dried with calcium chloride. After removal of the solvent, the residue was distilled in vacuum to give the ketones at once in a fairly pure state. The reaction must be performed in a single day without leaving overnight.

Methyl β-chlorovinyl ketone. Reaction of 18 g glacial acetic acid and 13 g silicon tetrachloride with acetylene in presence of 60 g aluminum chloride for 6 hours gave 9 g (30 %) of methyl β-chlorovinyl ketone.

B. p. 44.5–45.5° (27 mm), n^{20}_D 1.4642, d^{20}_4 1.1180, MR_D 26.05. C_4H_5OClF Calc. 25.1.

Found %: C 46.14, 46.13; H 4.91, 4.92. C_4H_5OCl. Calculated %: C 45.97; H 4.82.

According to the literature [9]: b. p. 38–39° (18–20 mm), n^{20}_D 1.4683, d^{20}_4 1.1198; according to the literature [1]: b. p. 40–41° (24 mm); n^{20}_D 1.4675.

Ethyl β-chlorovinyl ketone. From 22.2 g propionic acid, 13 g silicon tetrachloride and acetylene in presence of 60 g aluminum chloride for 4½ hours. Yield 12 g (34 %) of ethyl β-chlorovinyl ketone.

B. p. 59–60° (29 mm), n^{20}_D 1.4660, d^{20}_4 1.0761, MR_D 30.73. C_5H_7OClF. Calc. 29.70.

Found %: C 50.68, 50.65; H 6.00, 6.03. C_5H_7OCl. Calculated %: C 50.63; H 5.95.
According to the literature [1] : b. p. 55–56° (27 mm), n^{23}_D 1.4596, d^{23}_4 1.0702.

n-Propyl β-chlorovinyl ketone. From 24.6 g n-butyric acid and 13 g silicon tetrachloride in presence of 60 g aluminum chloride with passage of acetylene for 4½ hours. Yield 16 g (41 %) n-propyl β-chlorovinyl ketone.

B. p. 63.5° (16 mm), n_D^{20} 1.4648, d_4^{20} 1.0431, MR_D 35.13. C_6H_9OClF. Calc. 34.32.

Found %: C 54.43, 54.48; H 6.85, 6.91. C_6H_9OCl. Calculated %: C 54.36; H 6.84.

According to the literature [1]: B. p. 56–57° (12 mm), n_D^{20} 1.4640, d_4^{20} 1.0396.

n-Amyl β-chlorovinyl ketone. From 17.4 g n-caproic acid and 7 g silicon tetrachloride in presence of 30 g aluminum chloride with passage of acetylene for 4 hours. Yield 8 g (33 %) of n-amyl β-chlorovinyl ketone.

B. p. 94–95° (15 mm), n_D^{20} 1.4652, d_4^{20} 1.0014, MR_D 44.40. $C_8H_{13}OClF$. Calc. 43.55.

Found %: C 59.83, 59.97; H 8.10, 8.03. $C_8H_{13}OCl$. Calculated %: C 59.82; H 8.16.

According to the literature [10]: B. p. 87–88° (12 mm), n_D^{20} 1.4615, d_4^{20} 0.9960.

SUMMARY

1. Silicoanhydrides of saturated monobasic organic acids enter into reaction with acetylene in presence of anhydrous aluminum chloride in a medium of carbon tetrachloride, forming alkyl β-chlorovinyl ketones in yields of 30-41 %.

2. The reaction goes in accordance with a scheme involving two successive steps—addition of tetraacyloxysilane to acetylene with formation of ester of orthosilicic acid and alkyl β-hydroxy vinyl ketone, and cleavage of the latter under the action of aluminum chloride with formation of the corresponding alkyl β-chlorovinyl ketone.

LITERATURE CITED

[1] A. N. Nesmeyanov, N. K. Kochetkov and M. I. Rybinskaya, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1950, 350.

[2] N. K. Kochetkov, Prog. Chem. USSR 24, 32 (1955).

[3] Yu. K. Yuryev and G. B. Elyakov, Proc. Acad. Sci. USSR 86, 337 (1952).

[4] Yu. K. Yuryev and G. B. Elyakov, Proc. Acad. Sci. USSR 102, 763 (1955).

[5] Yu. K. Yuryev and G. B. Elyakov, J. Gen. Chem. 26,2350 (1956).*

[6] Yu. K. Yuryev, G. B. Elyakov and A. N. Vysokosov, J. Gen. Chem., 26, 926 (1956).*

[7] I. L. Kondakov, Syntheses Under the Influence of Zinc Chloride in the Aliphatic Series (Warsaw 1894).

[8] C. Hartmann and L. Gattermann, Ber. 25, 3531 (1892).

[9] A. Ya. Yakubovich and E. N. Mekulova, J. Gen. Chem. 16, 55 (1946).

[10] N. K. Kochetkov, A. Gonsales and A. N. Nesmeyanov, Proc. Acad. Sci. USSR 79, 609 (1951).

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[illegible]

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Found %: [illegible]

According to the literature [1]: [illegible]

[illegible]

[illegible]

According to the literature [illegible]

SUMMARY

1. [illegible]

2. [illegible]

[1] [illegible]

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[3] Yu. K. Yur'ev [illegible]

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[5] Yu. K. Yur'ev and [illegible]

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[9] A. Yu. [illegible]

[10] [illegible]

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THE CHEMISTRY OF SELENOPHENE

V. SELENOPHENE-2-ALDEHYDE, SELENOPHENE-2-CARBINOL AND SELENOPHENE-2-ACRYLIC ACID

Yu. K. Yuryev and N. N. Mezentsova

In previous investigations one of us showed that selenophene [1] and 3,4-dimethylselenophene [2] are easily acylated by silicoanhydrides of saturated monobasic organic acids in presence of anhydrous tin chloride, forming the corresponding ketones. Acylation of selenophene with silicoanhydrides of acid ethyl esters of dibasic acids under the same conditions gives ketoacids of the selenophene series [3].

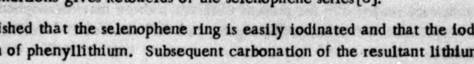
It was also established that the selenophene ring is easily iodinated and that the iodides are readily metalated by the action of phenyllithium. Subsequent carbonation of the resultant lithium-selenophenes leads to carboxylic acids of the selenophene series. By this route we obtained selenophene-2-carboxylic, 3-methylselenophene-2-carboxylic, 2,4-dimethyl-selenophene-5-carboxylic and 3,4-dimethylselenophene-2-carboxylic acids [4].

The literature of recent years contains reports of the synthesis of aldehydes in a series of five-membered nitrogen- and sulfur-containing heterocyclic compounds by formylation of their ring with dimethylformamide in presence of phosphorus oxychloride. This method was applied to the preparation of pyrrole-2-aldehyde [5], 1-methylpyrrole-2-aldehyde [6], indole-3-aldehyde [7] and thiophene-2-aldehyde [8].

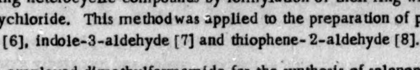
In the present work we employed dimethylformamide for the synthesis of selenophene-2-aldehyde • which has not previously been described in the literature.

Formylation of selenophene with dimethylformamide went smoothly and selenophene-2-aldehyde was obtained in 75 % yield.

Oxidation of selenophene-2-aldehyde with hydrogen peroxide gave selenophene-2-carboxylic acid:

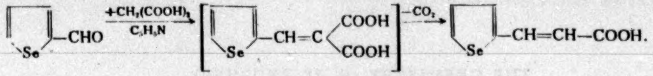


Selenophene-2-aldehyde entered with facility into the reactions characteristic of aldehydes of the aromatic series. Thus, heating of selenophene-2-aldehyde with acetic anhydride and anhydrous sodium acetate gave selenophene-2-acrylic acid:

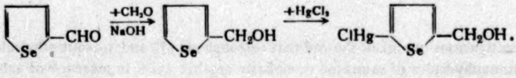


• Formylation of the selenophene ring in 3,5-diarylselenophenes with N-methylformanilide has been described in the literature. This enabled the preparation of some 2-formyl-3,5-diarylselenophenes: 2-formyl-3,5-diphenylselenophene, 2-formyl-3-5-di-p-tolylselenophene and 2-formyl-3,5-di-p-methoxyphenylselenophene [9].

This acid was also obtained by condensation of selenophene-2-aldehyde with malonic acid in presence of pyridine and subsequent decarboxylation of the resultant α-carboxy-β-(2-selenophene)-acrylic acid:



Reduction of selenophene-2-aldehyde with formaldehyde under the conditions of the Tishchenko-Cannizzaro reaction gave selenophene-2-carbinol. Mercuration of the latter led to 5-chloromercuriselenophene-2-carbinol:



The above reactions were realized in the present work and showed that selenophene-2-aldehyde undergoes the main reactions typical of aldehydes possessing an aromatic character — furfural, thiophene-2-aldehyde and benzaldehyde.

EXPERIMENTAL

Selenophene-2-aldehyde. 31.0 g (0.2 mole) phosphorus oxychloride was added with stirring and water cooling to a mixture of 21 g (0.16 mole) selenophene (b. p. 110-111° at 753 mm, n_D^{20} 1.5640, d_4^{20} 1.5250) and 14.8 g (0.2 mole) dimethylformamide in a three-necked flask fitted with stirrer, dropping funnel and reflux condenser with calcium chloride tube. The reaction mixture was then heated 1 hour on a water bath at 65° cooled, and poured on to ice (400 g) to which was added 300 g sodium acetate with stirring. The mixture was then heated to the boil, cooled and repeatedly extracted with ether. The combined ether extracts were dried with anhydrous sodium sulfate. After removal of the ether the reaction product was distilled in vacuum to give 19.1g(70%) selenophene-2-aldehyde:

B. p. 86–87° (7 mm), n_D^{20} 1.6292, d_4^{20} 1.6688, MR_D 33.87. $C_5H_4OSe\overline{F}_2$. Calc. 32.77.

Found %: C 38.04, 38.08; H 2.78, 2.66. C_5H_4OSe. Calculated %: C 37.75; H 2.53.

Selenophene-2-aldehyde semicarbazone was obtained by reacting 1.6 g aldehyde in 10 ml water with 1 g semicarbazide hydrochloride with heating on a boiling water bath; m. p. 205° (from aqueous alcohol). Yield quantitative (2 g).

Found %: N 19.16, 19.27. $C_6H_5ON_3Se$. Calculated %: N 19.57.

Selenophene-2-aldehyde thiosemicarbazone was similarly prepared from 1.6 g aldehyde and 1.2 g thiosemicarbazide hydrochloride; m. p. 176° (from aqueous alcohol. Yield quantitative (2.1 g).

Found %: N 17.59, 17.54. $C_6H_7N_3SSe$. Calculated %: N 18.0.

Selenophene-2-aldehyde 2,4-dinitrophenylhydrazone was prepared from 0.5 g of the aldehyde in 20 ml alcohol by treatment with 0.6 g of 2,4-dinitrophenylhydrazine in 2 ml concentrated sulfuric acid with addition of 3 ml water and 10 ml alcohol; m. p. 240° (from pyridine). Yield quantitative (1 g).

Found %: N 16.46, 16.27. $C_{11}H_8O_4N_4Se$. Calculated %: N 16.51.

Oxidation of selenophene-2-aldehyde. To a solution of 1.0 g aldehyde in 10 ml water was gradually added 6 ml 30% hydrogen peroxide with heating (about 100°). The aqueous solution was evaporated to 1/3 of its volume and extracted with ether; removal of the ether left 0.6 g (57%) of selenophene-2-carboxylic acid which after recrystallization from water melted at 120°; a mixture with selenophene-2-carboxylic acid prepared by metalation of 2-iodo-selenophene followed by carbonation of the resultant lithiumselenophene [4] did not give a depression of melting point: m. p. 120°.

Selenophene-2-acrylic acid: a) A mixture of 4.8 g (0.03 mole) selenophene-2-aldehyde, 5.2 g (0.05 mole) acetic anhydride and 5.6 g (0.08 mole) anhydrous sodium acetate was heated 10 hours on an oil bath at 195-200° in a flask with a reflux condenser. After cooling, 3 g sodium carbonate in 10 ml water was added to the flask. Selenophene-2-acrylic acid was precipitated from the aqueous solution of the salt with hydrochloric acid. Yield 3.5 g (60%) of selenophene-2-acrylic acid with m. p. 144° (from water).

Found %: C 41.74. 41.63; H 3.18, 3.19. $C_7H_6O_2Se$. Calculated %: C 41.80; H 3.00.

b) A mixture of 4.8 g (0.03 mole) selenophene-2-aldehyde, 3.12 g (0.03 mole) malonic acid and 3 ml dry pyridine was refluxed 4 hours in a flask on a water bath. Then 50 ml saturated sodium carbonate solution was added, and the unchanged aldehyde and pyridine were distilled off with steam. Acidification of the residue in the flask with hydrochloric acid gave selenophene-2-acrylic acid; m. p. 144°. Yield 4.5 g (75%). A mixed specimen with selenophene-2-acrylic acid obtained in the preceding experiment did not show a depression of melting point: m. p. 144°.

Selenophene-2-carbinol. a solution of 12 g sodium hydroxide in 12 ml water was added with stirring and heating on a water bath at 65° to a mixture of 10.6 g (0.066 mole) selenophene-2-aldehyde in 22 ml anhydrous methyl alcohol and 11 ml 40% formalin in a three-necked flask fitted with stirrer, dropping funnel and reflux condenser. The reaction mixture was heated 30 minutes, poured onto ice (150 g) and extracted with benzene (3 lots of 40 ml each). After drying with anhydrous sodium sulfate and distilling off the benzene, the residue was distilled in vacuum to give 7.4 g (70%) of selenophene-2-carbinol:

B. p. 120–121° (18 mm), 99° (5 mm), n^{20}_{D} 1.5985, d^{20}_{4} 1.6182, MR_D 34.44. $C_5H_6OSeF_2$.

Found %: C 37.55, 37.50; H 3.96, 3.99. C_5H_6OSe. Calculated %: C 37.28; H 3.75.

Selenophene-2-carbinol phenylurethane was prepared by heating equal volumes (0.2 ml each) of phenylisocyanate and carbinol: m. p. 82° (from ligroine). Yield quantitative.

Found %: N 5.46, 5.37. $C_{12}H_{11}O_2NSe$. Calculated %: N 4.99.

5-Chloromercuriselenophene-2-carbinol was obtained by reacting 1.08 g (0.0068 mole) selenophene-2-carbinol in 10 ml water with 50 ml of 5% aqueous solution of mercuric chloride: m. p. 195° (from water). Yield quantitative (2.3 g).

Found %: Hg 50.57. $C_5H_5OClHgSe$. Calculated %: Hg 50.89.

SUMMARY

1. Formylation of selenophene with dimethylformamide in presence of phosphorus oxychloride leads to preparation of selenophene-2-aldehyde (not described in the literature), which possesses the typical properties of an aromatic aldehyde.

2. Condensation of selenophene-2-aldehyde with acetic anhydride, and also with malonic acid, leads to selenophene-2-acrylic acid.

3. Selenophene-2-aldehyde is oxidized to selenophene-2-carboxylic acid with hydrogen peroxide, and is reduced to selenophene-2-carbinol with formaldehyde in presence of caustic alkali.

LITERATURE CITED

[1] Yu. K. Yuryev and G. B. Elyakov, Proc. Acad. Sci. USSR 102, 763 (1955).

[2] Yu. K. Yuryev and N. K. Sadovaya, J. Gen. Chem. 26, 930 (1956).*

[3] Yu. K. Yuryev, G. B. Elyakov and Z. V. Belyakova, J. Gen. Chem 26, 2353 (1956).*

[4] Yu. K. Yuryev and N. K. Sadovaya, J. Gen. Chem. 26, 3154 (1956).*

[5] R. Silberstein, J. Am. Chem. Soc., 76, 4485 (1954).

[6] E. Riskiewicz, R. Silberstein, J. Am. Chem. Soc. 76, 5802 (1954).

[7] G. Smith, J. Chem. Soc. 1954, 3842.

[8] E. Compaigne, J. Am. Chem. Soc. 75, 989 (1953).

[9] P. Demersemann and Ng. Buu-Noi, J. Chem. Soc. 1954, 4193.

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Moscow State University

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SALTS OF BIS-QUARTERNARY AMMONIUM BASES

B. V. Matveev and M. Z. Zalmanovich

Much attention has recently been paid to the synthesis of compounds with curare-like activity [1]. Curarizing activity is reported in the literature for bis-quaternary ammonium salts of polymethylene hydrocarbons [2-8]. These publications refer to the curare-like activity of bromides and iodides of bis-trimethyl and bis-triethyl bases of polymethylene hydrocarbons [2,3]; mention is also made of the anticancerogenic activity of salts of cyclic bis-quaternary ammonium bases [4]. All compounds of this type, whose synthesis and pharmacological activity are described in the literature, are derivatives of saturated normal hydrocarbons.

It was to be expected that the pharmacological activity of bis-quaternary ammonium salts might be considerably enhanced by the introduction of a double bond into the hydrocarbon chain. It was also of interest to study the influence of the structure of the hydrocarbon chain on the properties of the compounds prepared. Only one representative of compounds of this class, containing a double bond in the hydrocarbon chain between the nitrogen atoms, is known — (1,4)-bis-trimethyl-ammonium butene-2-hydroxide (I) [9]:

$$(CH_3)_3N-CH_2-CH=CH-CH_2-N(CH_3)_3^{2+} \quad 2(OH)^- .$$

(I)

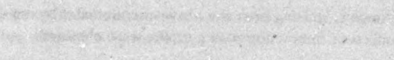
In this connection an objective of the work was the preparation of homologs of this compound containing one or two methyl groups at various carbon atoms.

EXPERIMENTAL

The following starting substances were used: 1,4-dibromopentene-2; 1,4-dibromo-2-methylbutene-2; 2,5-dibromohexene-3 and 1,4-dibromo-2,3-dimethylbutene-2, which were obtained by bromination of the corresponding dienic hydrocarbons (piperylene, isoprene, dipropenyl and diisopropenyl) in carbon tetrachloride or in chloroform [10].

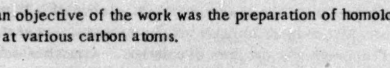
Into a solution of each of the above-mentioned dibromo compounds in benzene, cooled with iced water, was run a benzene solution of trimethylamine (4 moles amine to 1 mole dibromo compound). The reaction mixture was placed in an ampoule which was sealed and held at room temperature for 15-20 days. The reaction product, which separated in the form of colorless crystals, was pressed on a filter, repeatedly washed with dry benzene and dried in a vacuum-desiccator.

The following were prepared: 1,4-bis-(trimethylammonium-pentene-2 (II); (1,4)-bis-(trimethylammonium)-2-methylbutene-2 bromide (III); (2,5)-bis-(trimethylammonium)-hexene-3 bromide (IV) and (1,4)-bis-(trimethylammonium)-2,3-dimethylbutene -2 bromide (V):



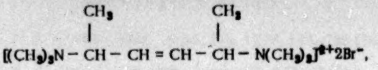
$$[(CH_3)_3N-\overset{\overset{\displaystyle CH_3}{|}}{C}H-CH=CH-CH_2-N(CH_3)_3]^{2+}\ 2Br^- ,$$

(II)

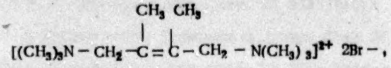


$$[(CH_3)_3N-CH_2-\overset{\overset{\displaystyle CH_3}{|}}{C}=CH-CH_2-N(CH_3)_3]^{2+}\ 2Br^- ,$$

(III)



$$[(CH_3)_3N-\overset{CH_3}{\overset{|}{C}H}-CH=CH-\overset{CH_3}{\overset{|}{C}H}-N(CH_3)_3]^{2+}2Br^-,$$ (IV)



$$[(CH_3)_3N-CH_2-\overset{CH_3}{\overset{|}{C}}=\overset{CH_3}{\overset{|}{C}}-CH_2-N(CH_3)_3]^{2+}\ 2Br^-,$$ (V)

All these compounds form colorless crystals, readily soluble in water, less soluble in alcohol, sparingly soluble in benzene and insoluble in ether.

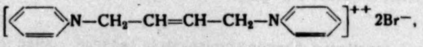
Results of analysis of these substances for bromine (Carius) and nitrogen (Dumas) contents are presented in Table 1.

TABLE 1

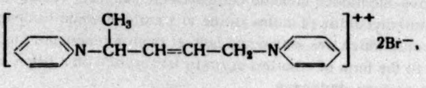
Substance	Found (%)		Calculated		
	Br	N	Empirical formula	Br (%)	N (%)
(II)	46.22	8.04, 8.01	$C_{11}H_{26}N_2Br_2$	46.24	8.09
(III)	—	8.18, 8.14	$C_{11}H_{26}N_2Br_2$	46.24	8.09
(IV)	43.80, 43.98	7.70, 7.60	$C_{12}H_{28}N_2Br_2$	44.44	7.77
(V)	44.43, 44.32	7.35, 7.71	$C_{12}H_{28}N_2Br_2$	44.44	7.77

In another series of experiments, starting from the above-mentioned dibromo derivatives as well as from 1,4-dibromobutene-2, products of interaction with pyridine were obtained.

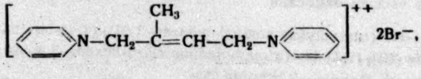
0.05 mole of the dibromo compound was run cautiously into a solution of 0.10 mole pyridine in anhydrous alcohol. The mixture was placed in an ampoule which was sealed and kept at room temperature for 3-4 days; the reaction product came down in the form of colorless crystals which were pressed on a filter, carefully and repeatedly washed with absolute ether, and dried in a vacuum desiccator. The yield of crystalline product reached 90-95 %. Bromides of 1,4-bis-pyridinium-butene-2 and its homologs were thus prepared:



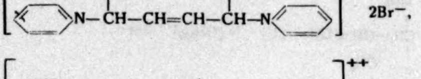
(VI)



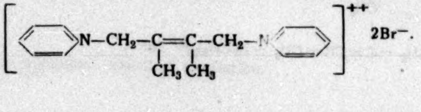
(VII)



(VIII)



(IX)



(X)

They all had good solubility in water, not so good in alcohol and benzene; they were insoluble in ether. Results of determinations of bromine and nitrogen are presented in Table 2.

TABLE 2

Substance	Found (%)		Calculated		
	Br	N	Empirical formula	N (%)	Br (%)
(VI)	42.79, 43.04	7.93, 8.12	$C_{14}H_{16}N_2Br_2$	7.53	43.01
(VII)	41.42, 41.65	7.88, 7.80	$C_{15}H_{18}N_2Br_2$	7.25	41.45
(VIII)	41.20, 40.90	7.26	$C_{15}H_{18}N_2Br_2$	7.25	41.45
(IX)	40.17, 39.40	7.42, 6.95	$C_{16}H_{20}N_2Br_2$	7.00	40.00
(X)	39.64, 39.61	6.97, 7.25	$C_{16}H_{20}N_2Br_2$	7.00	40.00

The pharmacological examination of the preparations, carried out by Yu. N. Shanin and I. I. Baryshnikov confirmed in some measure the prediction made at the start of this paper. Introduction of a double bond into the hydrocarbon chain between the two nitrogen atoms of bis-pyridinium derivatives does indeed intensify the ganglion-blocking properties. The effect is the most marked with (1,4)-bis-pyridinium-pentene-2 bromide (VII). In addition, I. I. Baryshnikov observed the ability of substances (II), (III), (IV) and (V) to lower the blood pressure; the highest activity is here manifested by compound (IV).

SUMMARY

1. Syntheses were carried out for the first time of the following bromides: (1,4)-bis-trimethylammonium-pentene-2 bromide; (1,4)-bis-trimethylammonium-2-methylbutene-2 bromide; (2,5)-bis-trimethylammonium-hexene-3 bromide; (1,4)-bis-trimethylammonium-2,3-dimethylbutene-2. These compounds were also characterized. They all possess hypotensive activity.

2. The following alkylene-bis-pyridinium bromides were synthesized and characterized for the first time: (1,4)-bis-pyridinium-butene-2 bromide; (1,4)-pyridinium-pentene-2 bromide; (1,4)-bis-pyridinium-2-methylbutene-2 bromide; (2,5)-bis-pyridinium-hexene-3 bromide; (1,4)-bispyridinium-2,3-dimethylbutene-2 bromide. All these compounds possess ganglion-blocking properties.

LITERATURE CITED

[1] N. A. Preobrazhensky and E. I. Genkin, Chemistry of Organic Medicinal Substances* (State Chem. Press 1953), p. 282.

[2] R. B. Barlow and H. R. Ing, Nature (1948), 161, 718.

[3] W. D. Paton, Lancet, 256, 21 (1949).

[4] J. L. Hartwell and M. A. Pogorelskin, J. Am. Chem. Soc. 72, 2040 (1950).

[5] E. P. Taylor, J. Chem. Soc. 1951, 1150.

[6] E. P. Taylor, J. Chem. Soc. 1952, 142.

[7] R. Hazard, Bull. Soc. chim. 1953, No 3, 270.

[8] J. Marozak, J. Jacob, R. Epstein, M. Olomucki, Compt. rend., 236, 246 (1953).

[9] R. Willstatter, T. Wirth, Ber., 46, 537 (1913).

[10] A. G. Bergman, J. Russ. Chem. Soc., 52, 24 (1920).

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• In Russian.

They all had good solubility in water [illegible] results of determinations of [illegible] and [illegible].

[illegible]

[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
(V)	[illegible]	[illegible]	[illegible]
(VIII)	[illegible]	[illegible]	[illegible]
(IX)	[illegible]	[illegible]	[illegible]
(X)	[illegible]	[illegible]	[illegible]

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1. [illegible] were [illegible] for the first time [illegible] [illegible]. They all proved [illegible]

2. [illegible]

[1] H. A. [illegible] and E. J. [illegible], [illegible]

[2] K. S. [illegible]

[3] M. G. [illegible]

[4] [illegible]

[5] K. F. [illegible], J. Chem. Soc. [illegible]

[6] K. F. [illegible], J. Chem. Soc. [illegible]

[7] L. [illegible], Bull. Soc. [illegible]

[8] [illegible]

[9] [illegible]

[10] A. G. [illegible]

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* In Russian.

SYNTHESIS OF N-SUBSTITUTED METHACRYLAMIDES

I. CARBOXY- AND CARBALKOXYPHENYL-METHACRYLAMIDES

M. M. Koton, T. A. Sokolova and G. M. Chetykina

Carboxy- and carbalkoxyphenyl-methylacrylamides are polymerizable monomers and are of definite interest in this respect. Only the ortho- and para-isomers of carboxyphenyl-methacrylamides are described in the literature. According to patent claims [1], they are obtained from the corresponding N-arylamides of β-chloroisobutyric acid by treatment with an aqueous solution of caustic alkali. The literature is lacking in any reference to the preparation of carbalkoxyphenyl-methacrylamides. At the same time interest in N-aryl- substituted methacrylamides has persisted to the present day. Thus, Patai and co-workers [2] obtained N-arylmethacrylamides by reacting equimolar amounts of methacrylic acid chloride with the corresponding aromatic amine. Another method of obtaining a series of N-aryl-methacrylamides has also been described [3, 4]. It consists in reacting ethyl magnesium bromide with aromatic amines and methyl methacrylate and is used for preparation of small amounts of aryl-methacrylamides.

For the synthesis of substituted amides of methacrylic acid we started from its acid chloride. Following the procedure of Patai [2], i.e., using equimolar amounts of acid chloride and aromatic amine, we found that the reaction in the present case does not go to the end due to part of the amine being used up in salt formation with release of hydrogen chloride during the reaction. We therefore preferred another method for the synthesis of carboxy- and carbalkoxyphenyl-methacrylamides. This is the method employed for the preparation of p-bromophenyl-methacrylamide [5] which involves reaction of 2 moles amine with 1 mole of methacrylic acid chloride.

The starting aminobenzoic acids and their esters possess a low basicity (K_{base} of the order of 10^{-12} [6-8]); their salts are therefore hydrolyzed with facility. The methacrylamides are therefore impure. They contain the starting amines and are difficult to purify. The amines evidently form molecular compounds with the methacrylamides which are not easily decomposed by treatment with hydrochloric acid. This is especially marked in the series of derivatives of m-aminobenzoic acid. This difficulty could be avoided by bringing into reaction an equimolar amount of a more basic tertiary amine. Thus, reaction of equimolar amounts of aminobenzoic acid ester, methacrylic acid chloride and dimethylaniline led to the carbalkoxyphenyl-methacrylamides in the pure form and in satisfactory yields. Lower yields of carboxyphenyl-methacrylamides are obtained in presence of dimethylaniline. Preparation of carboxyphenyl-methacrylamides necessitates reaction of 1 mole acid chloride with 2 moles aminobenzoic acid.

The prepared N-substituted methacrylamides were analyzed for their content of carbon, hydrogen and nitrogen by the method of microcombustion. The results of analysis and the properties of the carboxy- and carbalkoxyphenyl-methacrylamides are presented in the table. Melting points are corrected in all cases.

The starting amines for carboxyphenyl-methacrylamides were obtained by esterification of o-, m- and p-aminobenzoic acids by heating with methyl, ethyl or butyl alcohol saturated with dry hydrogen chloride. This method has been used on many occasions [9].

EXPERIMENTAL

Methacrylic acid chloride was prepared by reacting methacrylic acid (freshly distilled over copper powder in vacuum) with thionyl chloride (10 % over the theoretical amount). At the start the reaction went in the cold, but later the solution was heated for 8 hours at 60-80°. After heating, the mixture was twice recrystallized. Yield of fraction coming over at 97-99° about 80% of the theoretical (compare [10].)

Esters of aminobenzoic acids. 1 mole aminobenzoic acid was mixed with 15 moles alcohol in a flask with a reflux condenser. The reaction mixture, saturated with hydrogen chloride, was heated at the boil for 22-24 hours. At the conclusion of the reaction, the alcohol was distilled off in vacuum. After dissolving in a little water and treating with concentrated sodium carbonate solution until the reaction was alkaline, the precipitate was filtered, washed with water by decantation until neutral, and recrystallized from aqueous alcohol. When the ester was obtained in the form of oil, it was extracted with ethyl ether; the extract was dried over magnesium sulfate, and after evaporation of the ether it was distilled in vacuum. Esters were obtained in yields of 33 to 89%.

Carboxy- or carbalkoxyphenyl-methacrylamides. The starting amine, dimethylaniline in 10% excess over the theoretical amount, and benzene were placed in a two-necked round-bottomed flask fitted with a reflux condenser, a mechanical stirrer and a dropping funnel. Since the reaction products are easily polymerizable monomers, further heating was avoided by performing the reaction in ethereal solution. Addition was then made to the reaction mixture, dropwise and with stirring, of methacrylic acid chloride in the course of 1-2 hours. Since the starting amines have low basicity, only slight heat was developed by the acylation reaction. After all the acid chloride had been added, the mixture was stirred for another 1-2 hours and left overnight. The benzene was driven off from the solution in vacuum. The residual oil was treated with dilute hydrochloric acid and then with water; the N-substituted methacrylamide then came down in the form of crystals or remained in the form of oil. In the former case it was recrystallized from a suitable solvent. The oil was extracted with ether, the extract was dried, the ether was driven off, and the residue was distilled in vacuum. As mentioned above, in the case of meta-derivatives the treatment with hydrochloric acid must be repeated in order to decompose the molecular compounds of amine with final product.

p-Carboxyphenyl-methacrylamide (I) crystallizes from aqueous alcohol in the form of white needles with m. p. 215-216° Yield 60.4%. Soluble in alcohol, acetone, dioxane and dimethylformamide in the cold, in dichloro-ethane and water at the boil, insoluble in benzene and ether. The literature [1] gives m. p. 204-205° (with decomp.). The authors of the patent clearly had an impure product.

p-Carbomethoxyphenyl-methacrylamide (II) crystallizes from aqueous alcohol in the form of white needles with m. p. 134-134.5° Yield 58.4%. Soluble in alcohol, acetone, benzene, dichloroethane, ether and dimethylformamide in the cold, also in boiling water.

p-Carbethoxyphenyl-methacrylamide (III) crystallizes from aqueous alcohol in the form of white, quadratic prisms with m. p. 101.5-102°. Yield 60.7%. Soluble in acetone, alcohol, benzene, dichloroethane, dioxane, ether and dimethylformamide; partly soluble in boiling water.

The compound partly polymerizes when the synthesis is carried out in benzene. The pure amide is obtained in good yield when ether is used as solvent.

p-Carbobutoxyphenyl-methacrylamide (IV) crystallizes from gasoline or aqueous alcohol in the form of fine, white needles with m. p. 62.5-63°. Yield 55.3%. Soluble in alcohol, acetone, benzene, ether, dichloroethane and dioxane, sparingly soluble in gasoline, insoluble in water. It partly polymerizes during crystallization.

m-Carboxyphenyl-methacrylamide (V) crystallizes from aqueous alcohol in the form of fine crystals with m. p. 200.5-201° Yield 31.1%. Soluble in acetone, alcohol, dioxane, dimethylformamide and boiling water, insoluble in ether, benzene and dichloroethane.

m-Carbomethoxyphenyl-methacrylamide (VI) crystallizes from aqueous alcohol in the form of white plates with m. p. 77-77.5°. Yield 63.4%. Soluble in acetone, alcohol, ether, benzene, dichloroethane, dioxane and dimethylformamide, partly soluble in boiling water.

m-Carbethoxyphenyl-methacrylamide (VII) was first obtained in the form of an oil which came over in vacuum at 208-210° (5 mm). The distillate was stood in a desiccator over calcium chloride. After 1 1/2 months it crystallized to a reddish mass with a pleasant odor. Treatment with dilute hydrochloric acid gave a white precipitate without odor which was subjected to further purification. The amide crystallizes from gasoline in the form of long, white needles collected in clusters; m. p. 60.5-61°. Yield 33.9%. Soluble in acetone, alcohol, dioxane, ether, benzene, dichloroethane and dimethylformamide, poorly soluble in gasoline, insoluble in water.

o-Carboxyphenyl-methacrylamide (VIII) crystallizes from aqueous alcohol in the form of white, fine needles collected in clusters, m. p. 169-170°. Yield 59.3%. Soluble in acetone, alcohol, dioxane, ether and dimethylformamide in the cold, in benzene, dichloroethane and water at the boil.

o-Carbomethoxyphenyl-methacrylamide (IX) crystallizes from water and from aqueous alcohol in the form of colorless needles with m. p. 76-76.5°. Yield 38.8%. Soluble in acetone, benzene, alcohol, dioxane, ether, dichloroethane and dimethylformamide, poorly soluble in boiling water. Partly polymerizes during preparation.

o-Carbethoxyphenyl-methacrylamide (X) crystallizes from aqueous alcohol in the form of colorless needles with m. p. 54.5-55.5° Yield 27%. Soluble in acetone, alcohol, dioxane, benzene, ether, dichloroethane; partly soluble in boiling water. Partly polymerizes during preparation.

o-Carbobutoxyphenyl-methacrylamide (XI) was obtained in the form of an oil which was distilled in vacuum. The fraction collected at a vapor temperature of 173-175° (3 mm) partly crystallized on standing. The white plates were recrystallized from alcohol. M. p. 31.5-32°. Yield 38.5%. Soluble in acetone, alcohol, dioxane, ether, benzene, dichloroethane and dimethylformamide, insoluble in water. Partly polymerizes during distillation.

TABLE

Compound	Empirical formula	C content (%)		H content (%)		N content (%)	
		calculated	found	calculated	found	calculated	found
(I)	$C_{11}H_{11}O_3N$	64.39	64.21, 64.50	5.36	5.71, 5.74	6.82	6.46, 6.60
(II)	$C_{12}H_{13}O_3N$	65.75	65.56, 65.91	5.93	6.30, 6.17	6.39	6.34, 6.37
(III)	$C_{13}H_{15}O_3N$	66.95	66.99, 66.67	6.43	6.50, 6.49	6.01	5.90, 6.10
(IV)	$C_{15}H_{19}O_3N$	68.96	69.00, 69.30	7.28	7.28, 7.49	5.36	5.72, 5.85
(V)	$C_{11}H_{11}O_3N$	64.39	64.13, 64.05	5.36	5.25, 5.61	6.82	6.98, 7.09
(VI)	$C_{12}H_{13}O_3N$	65.75	66.17, 66.29	5.93	6.13, 6.18	6.39	6.38, 6.36
(VII)	$C_{13}H_{15}O_3N$	66.95	66.92, 66.61	6.43	6.37, 6.53	6.01	6.61, 6.57
(VIII)	$C_{11}H_{11}O_3N$	64.39	64.31, 64.86	5.36	5.87, 5.45	6.82	6.80
(IX)	$C_{12}H_{13}O_3N$	65.75	65.60, 65.86	5.93	6.40, 6.56	6.39	6.04, 6.23
(X)	$C_{13}H_{15}O_3N$	66.95	67.50, 67.58	6.43	6.53, 6.70	6.01	6.16, 6.10
(XI)	$C_{15}H_{19}O_3N$	68.96	68.84, 69.08	7.28	7.36, 7.56	5.36	5.98, 6.06

Note. Analyses were performed in the analytical laboratory of the Institute of High-Molecular Compounds of the Academy of Sciences USSR.

SUMMARY

1. o-, m- and p-Carbalkoxyphenyl-methacrylamides were prepared by a method based on reaction of 1 mole aminobenzoic acid or ester with 1 mole methacrylic acid chloride in presence of 1.1 mole dimethylaniline as an agent for binding the hydrogen chloride released.

2. m-Carboxyphenyl-methacrylamide and 8 carbalkoxyphenyl-methacrylamides were prepared for the first time and characterized.

LITERATURE CITED

[1] German Patent 753040 (1934); C. A., 3346 (1954).

[2] S. Patai, M. Bentov amd M. Reichman, J. Am. Chem. Soc. 74, 845 (1952).

[3] M. F. Bodroux, Bull. Soc. Chim. 33, 831 (1905).

[4] P. Bieber, Bull. Soc. Chim. No 1, 56 (1954).

[5] Bryant, Mitchell, J. Am. Chem. Soc. 60, 2748 (1938).

[6] Dictionary of Organic Compounds, I, 60 (1949).

[7] Beilstein, XIV, 422.

[8] Handbook of Chemistry, III, 506 (1952).

[9] H. C. Brill, J. Am. Chem. Soc. 43, 1320 (1921); A. Einhorn and M. Oppenheimer, Ann., 311, 158 (1900); E. H. Erdmann, Ber. 32, 1215 (1899); H. Schiff, Ann., 201, 366 (1880); T. Curtius and H. Melsbach, J. prakt. Chem. (2) 81, 542 (1910); E. Bamberger, Ann., 305, 362 (1899); G. Müller, Ber, 19, 1494 (1886); J. Estermann, Z. physiol. Chem. (B), 1, 148 (1928); H. Salkowski, Ber. 28, 1921 (1895); D. Vorlander and F. Meyer, Ann. 320, 135 (1902); M. P. Freundler, Bull. Soc. chim. (4) 1, 220 (1907); Synthesis of Organic Preparations* (Foreign Lit. Press, 1949), 2, 536.

[10] R. Fernandez and Cellini, C. A., 44, 8859 (1950).

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Institute of High-Molecular Compounds of
the Academy of Sciences of the USSR

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THE REACTION OF ACID CHLORIDES WITH SOME HYDROXYMETHYL COMPOUNDS

K. G. Mizuch, N. M. Kasatkin and Ts. M. Gelfer

It was previously shown that the course of acylation of N-hydroxymethyl-carbazole in a pyridine medium varies according to whether anhydrides or acid chlorides are used in the reaction. Acylation with the help of anhydrides led to quantitative formation of acyl derivatives; when using acid chlorides, acyl derivatives were obtained in small quantity, and dilution of the reaction mixture with water resulted in gradual separation of the original N-hydroxymethylcarbazole [1]. Treatment of N-hydroxymethylcarbazole with benzoyl chloride in CCl_4 later led to separation of an unknown substance (I), hydrolysis of which gave N-hydroxymethylcarbazole. It was found that (I) is readily soluble in water and on acidification is quantitatively transformed into N,N'-dicarbazylmethane; pyridine is formed on heating with caustic alkalies; it contains 11.6% chlorine (reaction with $AgNO_3$). No trace of benzoic acid was found, although it could have been formed by hydrolysis of (I) with water if the latter had been a product of addition of benzoyl chloride to N-hydroxymethylcarbazole. These results led us to re-examine the original theory of the structure of (I) and to suggest that the action of acid chlorides in presence of pyridine leads to replacement of the hydroxyl group of N-hydroxymethylcarbazole by chlorine with formation of the pyridinium salt of N-chloromethylcarbazole (I):

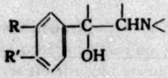
$$C_{12}H_8NCH_2OH + C_6H_5COCl + 2C_5H_5N \rightarrow$$

$$\underset{(I)}{[C_{12}H_8NCH_2 \cdot C_5H_5N]^+ Cl^-} + C_6H_5COOH \cdot C_5H_5N.$$

The structure of (I) was confirmed by determination of the molecular refraction; it accounts for the formation of N-hydroxymethylcarbazole on hydrolysis of (I). It is known that the structurally similar stearoylaminomethyl-pyridinium chloride is hydrolyzed in a similar fashion with formation of N-hydroxymethylstearamide [2].

Replacement of a hydroxyl group by chlorine under the action of chlorides of arylsulfonic acids in presence of tertiary amines has been repeatedly observed as a side reaction in the preparation of sulfonyl derivatives (survey of literature in [3]). The mechanism of this reaction was formulated by Hess and Stenzel [4] who suggested the intermediate formation of a sulfonyl compound which then reacts with the pyridine hydrochloride formed during the reaction. Other authors support this theory [5].

Replacement of hydroxyl by chlorine under the action of chlorides of carboxylic acids, which we observed in the case of N-hydroxymethylcarbazole, has been observed with an extremely limited number of compounds, mainly tertiary alcohols. Bretschneider and Biemann [6] showed that in compounds of the type of phenylalkanolamines, treatment with acetyl chloride can lead to



acylation of the hydroxyl of the side chain or to replacement by chlorine, depending upon the character of the substituents R and R'. The difference in behavior is due to migration of the electrons of the system under the influence of different R and R' which either cause loosening of the carbinol hydroxyl or strengthening of the C-OH bond.

Our observation of the replacement of the hydroxyl group of N-hydroxymethylcarbazole by chlorine must be viewed in relation to the previously established anomalous alkyl-oxygen cleavage of ethers of this compound on treatment with certain nucleophilic reactants [7]. In the present case the replacement of hydroxyl by chlorine must be regarded as a particular case of a general reaction of alkyl-oxygen cleavage at the basis of which lies the increased tendency, characteristic of compounds of this type, of the C-O bond to polarize in the $C^{+}-O^{-}$ direction. This theory makes the behavior of N-hydroxymethyl-3-nitro- and N-hydroxymethyl-3-benzoylcarbazole in acylation reactions understandable. Introduction of electrophilic substituents lowers the susceptibility of the C-O bond to polarization, and treatment with acid chlorides leads to formation of the normal products of acylation.

The structural characteristics governing the susceptibility of compounds of various types to alkyl-oxygen cleavage are not fully clarified. A series of compounds containing the $>NCH_2O-$ group is known to react according to this scheme with organomagnesium compounds, with alcohols and with amides [7, 8]. In the study of the replacement of hydroxyl by chlorine under the action of acid chlorides in presence of pyridine, we therefore in the first instance examined the behavior of N-hydroxymethyl compounds. It has been established [9] that N-hydroxymethylstearamide reacts similarly to N-hydroxymethylcarbazole and reacts with acetyl chloride and benzoyl chloride to form stearoylaminomethylpyridinium chloride (II). The reaction with sulfonic acid chlorides goes similarly (benzenesulfochloride and thionyl chloride).

Unlike N-hydroxymethylcarbazole and N-hydroxymethylstearamide, N-hydroxymethylphthalimide reacts in similar fashion, with formation of phthalimidomethylpyridinium chloride (III), only on treatment with sulfochlorides. The corresponding acyl derivatives were obtained on reaction with acetyl chloride and benzoyl chloride. The influence of a nucleophilic reactant on the reaction course was further demonstrated by reacting pyridine hydrochloride with N-hydroxymethyl derivatives of stearamide and phthalimide. In the case of N-hydroxymethylstearamide, (II) is formed with facility; under the same conditions N-hydroxymethylphthalimide remains unchanged.

The importance of the $>NCH_2O-$ grouping for realization of alkyl-oxygen cleavage was demonstrated by replacing this grouping by the $>NCH_2CH_2O-$ grouping. Thus, N-(β-hydroxyethyl)-phthalimide reacted with $C_6H_5SO_2Cl$ in presence of pyridine to form a sulfonyl derivative, while the benzoic ester of N-(β-hydroxyethyl)-carbazole, unlike the corresponding ester of N-hydroxymethylcarbazole [7], reacted with C_6H_5MgBr according to the normal scheme of acyloxygen cleavage.

Another series of hydroxymethyl compounds known to contain a highly labile hydroxyl are the α-hydroxymethylsulfones. The literature data, however, do not give us a clear picture of the types of nucleophilic reactants that lead to replacement of the hydroxyl. Thus, treatment of hydroxymethyl-p-tolylsulfone with ammonia or aniline leads to α-aminomethylsulfones [10], whereas the action of benzoyl chloride and pyridine gives p-tolylsulfonylmethyl benzoate [11].

For our investigation we made use of the readily accessible hydroxymethyl-p-acetamidophenylsulfone $CH_3CONHC_6H_4SO_2CH_2OH$ (IV), which, according to I. Kh. Feldman and Gavrilova [12] "has a very highly labile hydroxyl", readily reacting with amines. Reaction of (IV) with benzenesulfochloride in a pyridine medium gave two substances. One of them was insoluble in pyridine and was isolated by filtration of the reaction mixture. The second compound, isolated from the pyridine filtrate, was identified by analysis as a phenyl-sulfonyl derivative, hydroxymethyl-p-acetamidophenylsulfone

$$CH_3CONHC_6H_4SO_2CH_2OSO_2C_6H_5 \text{ (V).}$$

The pyridine-insoluble compound was purified by crystallization from aqueous alcohol. It is insoluble in alcohol and benzene, readily soluble in water; on heating it decomposes at above 250° without melting. Analytical data and the melting point of the picrate identified it as 1,1'-methylene-bis-(pyridiniumchloride)

(VI). This structure was finally confirmed by the identity of its picrate with the picrate obtained from 1,1'-methylene-bis- (pyridinium bromide); the latter was synthesized by the reaction of methylene bromide with an excess of pyridine. Formation of (VI) can be accounted for by the reaction of benzenesulfochloride and pyridine with formaldehyde, the latter originating from the hydroxymethyl-p-acetamidophenylsulfone. Experiments confirmed the possibility of such a transformation. Introduction of paraformaldehyde into a mixture of benzenesulfochloride and pyridine which was heated to 75° led to formation of 1,1'-methylene-bis-(pyridinium chloride) in a yield of about 75 %.

EXPERIMENTAL

Pyridinium salt of N-chloromethylcarbazole (I). 9.9 g N-hydroxymethylcarbazole was suspended in 70 ml CCl_4 and a mixture of 7.7 g benzoyl chloride, 8.7 g pyridine and 20 ml CCl_4 was added in the course of 15 minutes. The temperature of the mixture rose to 37°, and the N-hydroxymethyl-carbazole dissolved almost completely. The mixture was heated at 40° for 6 hours, then cooled and filtered. A precipitate of 11.7 g was collected. Evaporation of the filtrate gave 6.7 g substance which after crystallization from methanol melted at 97.6-98.4° and was identified from the melting point of a mixed sample as benzoyl-N-hydroxymethylcarbazole.

The CCl_4 -insoluble substance was treated at 40° with 30 ml toluene. Evaporation of the toluene filtrate gave 0.5 g of the original N-hydroxy-methylcarbazole. The toluene-insoluble substance was heated at 40° with twice the amount of acetone; part of the substance (1.23 g) did not dissolve and after purification from xylene was identified as carbazole.

The oil separating from the acetone filtrate formed colorless crystals (5.38 g) after prolonged freezing. The crystals melted at room temperature. They are soluble in water and extremely hygroscopic. The aqueous solution on standing gradually deposited N-hydroxymethylcarbazole with m. p. 129.2-130°. On heating an aqueous solution of the substance with 10% sodium hydroxide solution, pyridine was detected (formation of $[Cu(C_5H_5N)_2]\cdot[SCN]_2$). Subsequent acidification of the alkaline solution led to separation of N,N'-dicarbazylmethane. Not even traces of benzoic acid were found after extraction of the acid mother liquor with ether and evaporation of the solvent.

Addition of silver nitrate to an aqueous solution of the compound led to precipitation of silver chloride.

d_4^{20} 1.0496, n_D^{20} 1.5260, MR 86.18; Calc. 86.47.

Found %: Cl 11.6, 11.48. $C_{18}H_{15}N_2Cl$. Calculated %: Cl 12.03

Acidification of an aqueous solution of the compound with hydrochloric acid gave N,N'-dicarbazyl-methane with m. p. 311-312° (90.3% of theory).

Action of acid chlorides on N-hydroxymethyl derivatives of acid amides. Stearoylaminomethylpyridinium chloride (II). a) Action of benzenesulfochloride. 18.8 g N-hydroxymethylstearamide was suspended in 120 ml CCl_4 ; the suspension was heated to 40° and a mixture of 12 g benzenesulfochloride and 12 g pyridine was added. The mixture was heated at 55° for 3 hours and then cooled; the stearoylaminomethylpyridinium chloride (II) was then filtered off in admixture with a small amount of the pyridinium salt of benzenesulfonic acid (35.4 g). Purification of (II) was effected by crystallization from CCl_4 or acetone and presented difficulty due to the instability of (II). After crystallization from acetone the m. p. was 134.7-135°. (Literature data: chars at 92° melts at 135° [13]).

(II) is easily soluble in the cold in methanol and ethanol, soluble on heating in acetone and butanol, sparingly soluble in benzene and CCl_4 .

Found %: N 6.54, 6.72; Cl 8.46, 8.47. $C_{24}H_{43}ON_2Cl$. Calculated %: N 6.82; Cl 8.63.

(II) can be easily identified by quantitative transformation into the water-insoluble distearoylamino-methane. 0.5010 g stearoylaminomethylpyridinium chloride was heated with 5% sulfuric acid to give 0.3528 g (99.53%) distearoylaminomethane with m. p. 147.4-147.6° (from butanol). (Literature data: m. p.

147° [2]).

b) Action of benzoyl chloride. 6.26 g N-hydroxymethylstearamide in 50 ml CCl_4 was heated to 50° and a mixture of 3.38 g benzoyl chloride and 4.0 g pyridine was added. The reaction mixture was heated at 65° for 2 hours and then cooled; the crystals were filtered (9.4 g) and purified by crystallization from chloroform.

Found %: Cl 8.19, 8.19. $C_{24}H_{43}ON_2Cl$. Calculated %: Cl 8.63.

Distearoylaminomethane was obtained in quantitative yield by heating the substance with 5% sulfuric acid.

c) Action of thionyl chloride. 6.26 g N-hydroxymethylstearamide was suspended in 50 ml CCl_4 and heated to 40°; a mixture of 2.8 g thionyl chloride and 4.0 g pyridine was added, the temperature of the reaction mixture then rising to 63°. The mixture was heated at 65° for 4 hours and worked up as described under (b).

Found %: Cl 8.69, 8.68. $C_{24}H_{43}ON_2Cl$. Calculated %: Cl 8.63.

Heating of the substance with 5% sulfuric acid converted it quantitatively into distearoylaminomethane.

Phthalimidomethylpyridinium chloride (III). To a mixture of 165 ml pyridine and 32.5 g benzenesulfochloride was added 27 g N-hydroxymethylphthalimide. During this operation the temperature rose to 64° and the phthalimide dissolved completely. The reaction mixture was heated at 62-64° for 3 hours and stood overnight for completeness of precipitation. The precipitate, a mixture of phthalimidomethylpyridinium chloride and a little pyridinium salt of benzenesulfonic acid, was filtered. Yield 38.85 g, m. p. 220-223° Crystallization from butyl alcohol-acetone (70:30) raised the m. p. to 227-228°. (III) is readily soluble in water (10 g in 1 g water), methanol and ethanol, sparingly soluble in benzene, CCl_4 and acetone.

Found %: Cl 12.76, 12.69. $C_{14}H_{11}O_2N_2Cl$. Calculated %: Cl 12.91.

N-(Benzoyloxymethyl)-phthalimide. 8.85 g N-hydroxymethyl phthalimide was suspended in 80 ml CCl_4 and a mixture of 8.5 g benzoyl chloride, 10 g pyridine and 10 ml CCl_4 was added. The reaction mixture was heated at 65° for 6 hours. After cooling, the crystals were filtered off, m. p. 125-125.8°. After crystallization from methanol the m.p. rose to 126.8-127.8°.

Found %: C 68.8, 68.68; H 3.79, 4.1; N 4.96, 4.92. $C_{16}H_{11}O_4N$. Calculated %: C 68.32; H 3.94; N 4.98.

N-(Benzoyloxymethyl)-phthalimide was also obtained by the action of benzoic anhydride on N-hydroxymethylphthalimide in presence of pyridine. M. p. 125-125.8°.

Action of pyridine hydrochloride on N-hydroxymethylphthalimide. 2.2 g pyridine was dissolved in 50 ml CCl_4 and the solution saturated with hydrogen chloride. The excess of the latter was removed with a stream of dry air and 1 drop of pyridine was added to completely bind the HCl. Addition was then made of 4.42 g N-hydroxymethylphthalimide in 20 ml CCl_4 and the reaction mixture was heated at 55-60° for 3 hours. No change in the reaction mixture was observed. After cooling, the precipitate was filtered and washed with water. The product is insoluble in cold water and does not contain chlorine ions. Recrystallization from hot water gave N-hydroxymethylphthalimide with m. p. 139.6-140.5°.

N-(Benzoyl-β-hydroxyethyl)-phthalimide. 3.8 g N-(β-hydroxyethyl)-phthalimide with m. p. 129-129.5° was dissolved in 10 ml pyridine and with external cooling 2.8 g benzoyl chloride was added. Considerable heat was developed during the reaction. The reaction mixture was heated for 30 minutes on a boiling water bath, cooled, and poured onto ice. The crystals were filtered, washed with water (4.1 g) and recrystallized from a mixture of acetone and methyl alcohol. The product melted at 116.2-116.6°; its analysis showed it to be identical with N-(benzoyl-β-hydroxyethyl)-phthalimide. Soluble in benzene and methanol, sparingly soluble in acetone.

Found %: C 69.04, 69.05; H 4.76, 4.63; N 4.72, 4.64. $C_{17}H_{13}O_4N$. Calculated %: C 69.15; H 4.43; N 4.74.

N-(Phenylsulfonyl-β-hydroxyethyl)-phthalimide. 4.77 g N-(β-hydroxyethyl)-phthalimide was dissolved in 50 ml pyridine, and addition was made of 4.9 g benzenesulfochloride at 20°. The reaction went with appreciable rise of temperature. The reaction mixture was left until the next day; on dilution with water a white crystalline precipitate (5.3 g) came down; m. p. 136.5-137°. After recrystallization from methyl alcohol the m. p. was 138-138.5°. Elementary analysis confirmed that the substance was N-(phenylsulfonyl-β-hydroxyethyl)-phthalimide. Soluble in methyl alcohol and acetone.

Found %: C 57.64, 57.54; H 3.62, 3.84; N 4.31, 4.32; S 9.64, 9.70. $C_{16}H_{13}O_5NS$. Calculated %: C 57.99; H 3.95; N 4.23; S 9.68.

Action of phenylmagnesium bromide on N-(benzoyl-β-hydroxyethyl)-carbazole. To a cooled solution of phenyl magnesium bromide, prepared from 3.4 g magnesium and 19.8 g bromobenzene in 70 ml ether and separated from excess of magnesium, was gradually added 9.46 g N-(benzoyl-β-hydroxyethyl)-carbazole with m.p. 141.2-141.8°. After standing for 1 hour in ice, the reaction was brought to an end by heating of the reaction mixture at a gentle boil for 3 hours. It was then recooled and treated with saturated ammonium chloride solution. The ether layer was separated from the aqueous layer and the latter was extracted with ether. No benzoic acid was detected when the aqueous layer was acidified. The combined ether extracts were dried with sodium sulfate and evaporated to yield 15.1 g of yellowish substance which was extracted in the cold with gasoline. The gasoline-insoluble substance was twice recrystallized from benzene-gasoline (1:1). Yield 4.52 g (71.3 %) of β-hydroxyethylcarbazole with m. p. 79.5-80.5°. (Literature: 83-83.5° [14]).

Evaporation of the gasoline extract and recrystallization of the residue from chloroform gave 3.4 g (62.2 %) of benzophenone with m. p. 44.3-45.3°.

Reaction of benzenesulfochloride in presence of pyridine with hydroxymethyl-p-acetamidophenylsulfone (IV). 21.1 g benzenesulfochloride was gradually added to 70 ml pyridine with stirring and cooling. The mixture was stirred for 30 minutes at room temperature, then cooled to +5°; portionwise addition was then made of 22.93 g of (IV) with m. p. 162-163°; The temperature of the reaction mixture rose. During the addition of (IV) the temperature was held at 5-6° by external cooling. After (IV) had been added, the mixture was heated for 2 hours at 75° stirred for 5 hours, and then stood overnight at room temperature. The precipitate was filtered and washed with pyridine. The mother liquor was run into water. The resultant precipitate (the phenylsulfonyl derivative of hydroxymethyl-p-acetamidophenylsulfone (V), weighing 20.65 g, was recrystallized from ethanol and gave 12 g of crystals with m. p. 181-182°. After a second recrystallization from ethanol the m. p. was 185.2-186.5°.

Found %: C 48.82, 48.79; H 3.87, 3.86; N 3.78, 3.94; S 17.55, 17.66 (Liebig method). $C_{15}H_{15}O_6NS_2$. Calculated %: C 48.77; H 4.09; N 3.79; S 17.36.

1,1'-Methylene-bis-(pyridinium chloride) (VI). 1) The pyridine-insoluble precipitate (9.4 g) was recrystallized from a mixture of alcohol and water (9:3) and gave white crystals (4.15 g), readily soluble in water, insoluble in alcohol and benzene. Silver chloride came down when silver nitrate was added to the aqueous solution of the substance.

Found %: C 50.65, 50.72; H 5.49, 5.54; N 10.75, 10.82; Cl 26.8. $C_{11}H_{12}N_2Cl_2 \cdot H_2O$. Calculated %: C 50.59; H 5.40; N 10.73; Cl 27.15.

According to Schmidt [15], methylene-bis-(pyridinium chloride) crystallizes from aqueous alcohol with one molecule of water.

Mixing of aqueous solutions of the substance and picric acid resulted in precipitation of a sparingly soluble picrate with m. p. 245° (with decomp.). A mixture with the picrate obtained from 1,1'-methylene-bis-(pyridinium bromide) did not give a depression of melting point.

The aqueous alcoholic mother liquor obtained during the crystallization was evaporated and the residue dissolved in water. A further 2.1 g of 1,1'-methylene-bis-(pyridinium chloride) was isolated from this solution in the form of picrate.

2) To 70 ml pyridine was added 19.4 g benzenesulfochloride with stirring and cooling. The mixture was stirred 30 minutes at room temperature, after which 3.3 g 90% paraformaldehyde was added. The mixture was then heated for 1 hour to 75° and stirred at this temperature for 5 hours. The precipitate was filtered on the following day and washed with alcohol. The product was purified by crystallization from a mixture of alcohol and water (9:3) to give 9.72 g of 1,1'-methylene-bis-(pyridinium chloride) hydrate.

Found %: C 50.88, 50.61; H 5.38, 5.56; N 10.86, 10.79; Cl 27.0, 26.7 (by titration with $AgNO_3$). $C_{11}H_{12}N_2Cl_2 \cdot H_2O$. Calculated %: C 50.59; H 5.40; N 10.73; Cl 27.15.

Melting point of picrate 245-247° (with decomp.). A mixed specimen with the picrate obtained from 1,1'-methylene-bis-(pyridinium bromide) did not give a depression of melting point. An additional 1.1 g of (VI) was isolated from the aqueous alcoholic mother liquor, as indicated above, in the form of picrate.

1,1'-Methylene-bis-(pyridinium bromide). 3.48 g methylene bromide and 10 ml pyridine were heated for 5 hours on a boiling water bath. The precipitate was filtered off and washed with alcohol. Yield 5.2 g (78.3%) 1,1'-methylene-bis-(pyridinium bromide) with m. p. 255-259°. (Literature data: m. p. 255-258° (with decomp.) [16]).

The picrate was prepared by adding 50 ml of a cold saturated solution of picric acid to 0.33 g of 1,1'-methylene-bis-(pyridinium bromide) in 30 ml water. The mixture was heated to the boil and cooled. Weight of precipitated picrate 0.62 g; m. p. 245-246.5° (with decomp.). The literature reports m. p. 245-249° [17]; 239-240° (with frothing and decomposition) [16].

SUMMARY

The action of acid chlorides in presence of pyridine on some hydroxymethyl compounds was studied and the following facts were established.

1. The action of chlorides of carboxylic and sulfonic acids on N-hydroxymethylcarbazole and N-hydroxymethylcarbazole and N-hydroxymethylstearamide leads to pyridinium salts of the corresponding chloromethyl compounds.

2. N-Hydroxymethylpthalimide similarly reacts with sulfonic acid chlorides; its reaction with chlorides of carboxylic acids yields acyl derivatives.

3. Hydroxymethyl-p-acetamidophenylsulfone reacts with benzenesulfochloride and pyridine with formation of a phenylsulfonyl derivative and 1,1'-methylene-bis-(pyridinium chloride); the latter can be obtained in good yield by interaction of paraformaldehyde, benzenesulfochloride and pyridine.

LITERATURE CITED

[1] K. G. Mizuch and Ts. M. Gelfer, J. Appl. Chem. 19, 939 (1946).

[2] F. V. Davis, Soc. Dyers Colourists, 63, 260 (1947); H. A. Schuyten, J. W. Weaver, J. G. Frick and J. D. Reid, Textile Research J. 22, 424 (1952).

[3] R. S. Tipson, J. Org. Chem. 9, 235 (1944).

[4] K. Hess and H. Stenzel, Ber. 68, 981 (1935).

[5] A. C. Cope and M. Burg, J. Am. Chem. Soc. 74, 611 (1952); D. Klamann, Monatsh. 84, 54 (1953).

[6] H. Bretschneider and K. Biemann, Monatsh. 81, 31 (1950).

[7] K. G. Mizuch, J. Gen. Chem. 16, 1471 (1946); K. G. Mizuch and Ts. M. Gelfer, Proc. Acad. Sci. USSR, 79, 807 (1951).

[8] G. M. Robinson; R. Robinson, J. Chem. Soc., 123, 532 (1923); M. Senkus, J. Am. Chem. Soc., 67, 1515 (1945); E. D. Bergmann, D. Lavie, S. Pinchas, J. Am. Chem. Soc., 73, 5662 (1951); W. J. Burke, M. J. Kolbezen, C. W. Stephens, J. Am. Chem. Soc., 74, 3601 (1952); K. G. Mizuch, J. Gen. Chem. 23, 861 (1953); (T. p. 901)*; K. G. Mizuch and R. A. Lapina, J. Gen. Chem. 23, 1512 (1953)(T. p. 1583)*.

[9] K. G. Mizuch and N. M. Kasatkin, Author's Certificate No. 95061.

[10] C. M. Suter, Chemistry of Organic Compounds of Sulfur, part III. 132 (1951).

[11] L. Field and P. H. Settlage, J. Am. Chem. Soc. 73, 5870 (1951).

[12] I. Kh. Feldman and A. E. Gavrilova, J. Gen. Chem. 22, 286 (1952), (T. p. 347)*.

[13] J. W. Weaver, H. A. Schuyten, J. G. Frick, J. D. Reid, J. Org. Chem. 16, 1111 (1951).

[14] R. G. Flowers, H. F. Miller and L. W. Flowers, J. Am. Chem. Soc. 70, 3019 (1948).

[15] E. Schmidt, Chem. Zentr. 1913, I, 2139.

[16] F. Krohnke, Ber. 83, 56 (1950).

[17] L. C. King, J. Am. Chem. Soc. 70, 243 (1948).

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K. E. Voroshilov Institute of Research
for Organic Intermediates and Dyes

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REACTIONS OF ACYL PEROXIDES WITH MERCURY

G. A. Razuvaev and Yu. A. Oldekop

We previously showed [1] that radicals formed on decomposition of peroxides can be fixed by metallic mercury. On carrying out the reaction at low temperatures, $RCO_2\cdot$ radicals are fixed at the mercury with formation of mercurous salts, while at higher temperature the $RCO_2\cdot$ radicals break down to $R\cdot$ and CO_2 with formation of RHgOCOR. The medium in which these reactions take place plays an important part. The cases that we investigated involved competitive reactions of acyl peroxides with mercury and solvent. In the present work we studied the reactions of acyl peroxides with mercury in various media and extended the scope to cover, apart from benzoyl and acetyl peroxides, also chloroacetyl and m-nitro-benzoyl peroxides; the two latter give more stable $RCO_2\cdot$ radicals on break down.

Our solvents may be divided into three classes: 1) those reacting less readily with peroxides than with mercury; 2) those reacting with peroxide with greater facility than with mercury; 3) solvents entering into reaction with mercury as a result of initiation by peroxide. Benzene and dioxane belong to the first group. Acetyl peroxide reacts in a benzene medium with mercury at the ordinary temperature with liberation of CO_2 and with formation of mercurous acetate. Methyl mercuric acetate was not detected even in traces. (It was previously observed [1, 2] that a considerable amount of methyl mercuric oxide is formed on heating.) Chloroacetyl peroxide reacts in the same manner. On shaking its benzene solution with mercury at the ordinary temperature, fixation of the chloroacetyloxy radical at the mercury is observed; 97% of mercurous chloroacetate was isolated. It is interesting to note that the direction of the reaction is not changed even when the reaction is conducted in boiling benzene, only the velocity increasing considerably. 70% of mercurous chloroacetate was isolated. The $ClCH_2CO_2\cdot$ radical only broke down to an insignificant extent. The extent of decomposition was determined from the amount of CO_2 released, and was found to be 2.5%. We therefore see that the introduction of chlorine greatly stabilizes the $RCO_2\cdot$ radical. A similar effect is exerted by the nitro group on the stability of $O_2NC_6H_4CO_2\cdot$ which is more stable than the $C_6H_5CO_2\cdot$ radical. A high yield of mercurous m-nitrobenzoate is obtained at the ordinary temperature. With rising temperature the yield of mercurous salt falls sharply, but formation of m-nitrophenyl mercury is not observed. With rising temperature the peroxide probably starts to react with the solvent. Dioxane occupies an intermediate position between the 1st and 2nd group. On shaking a dioxane solution of benzoyl peroxide with mercury at the ordinary temperature, mercurous benzoate is formed but only in 30% yield.

The second group of solvents includes alcohols which are known to react with facility with acyl peroxides (apart from tertiary). We observed that the addition of hydroquinone to a benzene solution of benzoyl peroxide leads to complete suppression of the reaction of the peroxide with mercury both in the cold and with heating. In a solution of ethylene glycol monoethyl ether, peroxides do not react with mercury. Thus, m-nitrobenzoyl peroxide did not react at all with mercury even when the solvent was boiled.

Carbon tetrachloride belongs to the 3rd group of solvents. Chlorination of mercury is observed [1] when acetyl peroxide is heated with this solvent. Heating of benzoyl peroxide in carbon tetrachloride with mercury gives phenylmercuric chloride [3]. But if the reaction between mercury and benzoyl peroxide is performed in carbon tetrachloride at the ordinary temperature, no reaction between mercury and solvent is observed, and mercurous benzoate is formed. It may be suggested that the reaction between mercury and carbon tetrachloride is initiated by $R\cdot$ radicals and not by $RCO_2\cdot$ radicals. This theory may be checked by performing the reaction in carbon tetrachloride between mercury and m-nitrobenzoyl peroxide. As indicated above, the nitrobenzoyloxy radical does not break down with release of CO_2 even at relatively high temperatures. In this case, as was expected, we established only the formation of mercuric salts of nitrobenzoic acid. Very little CO_2 was evolved.

EXPERIMENTAL [*]

Reactions taking place without heating

Reaction of acetyl peroxide with mercury and benzene. 4.5 g acetyl peroxide in 100 ml benzene was shaken on a machine with 25 g mercury for 100 hours at room temperature. A test for peroxide gave a negative result. At the end of the reaction, the milky white precipitate was separated from metallic mercury and filtered from benzene. It was mercurous acetate (reactions with KI, NH_3, KCl, etc.); its weight was 13.4 g or 68 % calculated on the original peroxide.

Reaction of chloroacetyl peroxide with mercury in benzene. **Chloroacetyl** peroxide was prepared by a slight modification of the method of Vanino and Uhlfeder [4]. 20 g hydrogen peroxide (15%) was placed in a beaker and cooled to 0°. With constant cooling and stirring, slow addition was made of 5 g chloroacetyl chloride. The resultant peroxide in the form of a white crystalline solid was collected, quickly washed with iced water, dissolved in benzene, and dried with calcium chloride. The amount of peroxide was determined iodometrically in the benzene solution. The yield of chloroacetyl peroxide reached 2.2 g (53%). 1.5 g of the peroxide in solution in 50 ml benzene was stirred at room temperature for 2 hours. At the end of the experiment no free peroxide was detected in the reaction mass. The reaction yielded 4.5 g (97%) of mercurous chloroacetate (identified by reaction with KI, NH_3 and $CaCl_2$). M. p. 181°, which is confirmed by literature data.

Reaction of benzoyl peroxide with mercury in carbon tetrachloride. 2.42 g (0.01 mole) benzoyl peroxide (with relation to 100 percent peroxide)[**], 45 g of metallic mercury and 50 ml carbon tetrachloride were vigorously shaken at room temperature for 50 hours. The resultant whitish-grey, clotty mass was mechanically separated from the mercury and filtered. The solid was washed several times with hot CCl_4 and, after addition of 5 g KCl, steam was passed through (steam distillation is convenient for rapid elimination of solvent). After the distillation, 4.25 g (90 %) mercurous chloride was filtered off. The filtrate gave a positive reaction for divalent mercury. 0.3 g mercury chloride was obtained after precipitation with hydrogen sulfide. After removal of the latter, the residue was evaporated to a small volume and acidified with conc. HCl to bring down 2.1 g benzoic acid with m. p. 120-121° (from water).

Reaction of benzoyl peroxide with mercury and dioxane. 1 g benzoyl peroxide, 40 g metallic mercury and 20 ml dioxane were stirred at room temperature for 100 hours. The reaction mass was then filtered, the residue washed in alcohol and, after addition of excess calcium chloride, steam was passed through it. The residue from steam distillation, after filtration, yielded 0.57 g (29%) of mercurous chloride complex. Mercurous chloride was separated from the calcium salt of benzoic acid by the addition of concentrated HCl; the residue contained 0.5 g benzoic acid with m.p. 120°.

Reaction of benzoyl peroxide with mercury and hydroquinone in benzene. 1.21 g (0.005 mole) benzoyl peroxide, 0.55 g hydroquinone, 50 g mercury and 20ml benzene were shaken for 15 hours. The precipitate was filtered and the mercury separated, leaving 0.2 g quinhydrone. Benzene was removed from the filtrate by distillation; careful evaporation of the benzene yielded 0.1 g p-quinone with m. p. 111°. After distillation of the benzene the weight of residue was 1.3 g; steam was passed through this mass for a short period and a further 0.15 g quinone was collected with m. p. 111° (sublimation). The residue contained benzoic acid with m. p. 119-120° (from water).

Reaction of m-nitrobenzoyl peroxide with mercury in benzene. m-Nitrobenzoyl peroxide was prepared by nitration of benzoyl peroxide [5]. 1 g of m-nitrobenzoyl peroxide (activity 98%), 70 g metallic mercury and 20 ml benzene were shaken for 30 hours at room temperature.

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[*] N. K. Taikova and I. G. Malceneva participated in the experimental work.

[**] This also applies to the later experiments with benzoyl peroxide.

The reaction mass was then separated mechanically from mercury, washed several times with benzene and then subjected to steam distillation. To the residue was added a saturated solution of calcium chloride, and the distillation was continued. After completion of distillation the residue was filtered. The solid was mercurous chloride (blackening with concentrated ammonia), weight 1.25 g (90%). The filtrate was evaporated to a small volume. Crystals of calcium m-nitrobenzoate came down; weight 1.3 g. Aqueous methanol was added to this substance and HCl was passed through. On the following day needles of methyl m-nitrobenzoate came down; m. p. 78-79°.

Reactions taking place with boiling of the solvent

Reaction of chloroacetyl peroxide with mercury in benzene. 1.2 g chloroacetyl peroxide in 50 ml benzene was stirred with 25 g mercury at the boiling point of benzene for 2 hours. At the conclusion of the reaction, a test for peroxide was negative. The mercury was separated and the precipitate decanted. The precipitate was filtered from benzene. Investigation showed that it was mercurous chloroacetate (reaction for mercurous ion with KI, NH_3 and KCl), m. p. 180°. Weight 2.6 g (70%). CO_2 was collected during the reaction (absorption in barytes water). Weight of $BaCO_3$ 0.08 g, corresponding to 2.5% of decomposed peroxide.

Reaction of benzoyl peroxide with mercury and hydroquinone in benzene. 2.42 g benzoyl peroxide, 1.1 g hydroquinone, 60 g mercury and 40 ml benzene were shaken while the benzene was boiled for 15 hours. At the end of the reaction, the quinhydrone (0.45 g) was filtered off. The filtrate was distilled; the solvent was distilled off and steam was passed through the residue for a short time to eliminate the residue of benzene. The residue contained 2.4 g benzoic acid. From the benzene solution, after evaporation of the benzene, was collected 0.55 g p-quinone.

Reaction of m-nitrobenzoyl peroxide with mercury in benzene. 3.3 g m-nitrobenzoyl peroxide (activity 98%), 100 g metallic mercury and 50 ml benzene were heated at the boiling point of benzene with vigorous stirring for 6 hours. Half an hour after the start of reaction, the mass thickened and changed into a dirty-grey cream. Owing to the difficulty of filtering such a mass, the mercury was mechanically separated, saturated calcium chloride solution was added, and steam was passed through. After the benzene had been driven off, distillation with steam was continued for a short time. On completion of the distillation, the precipitate was filtered. It consisted of mercurous chloride blackening with concentrated ammonia), and its weight after separation of the mercury was 1 g (22%). The filtrate contained calcium benzoate. Weight of dry salt 2.75 g.

Reaction of m-nitrobenzoyl peroxide with mercury in carbon tetrachloride. 3.32 g m-nitrobenzoyl peroxide (activity 98%), 50 ml carbon tetrachloride and 25 g mercury were shaken while the solvent was boiled for 18 hours. The thick reaction mass was separated from the mercury, filtered, and repeatedly washed with hot carbon tetrachloride. The precipitate was thereupon treated with saturated calcium chloride solution. 3.7 g (80%) mercurous chloride was obtained. During the experiment 0.018 g CO_2 came off, equivalent to 2% of the peroxide taken into reaction.

Reaction of m-nitrobenzoyl peroxide with mercury in ethylene glycol monoethyl ether. 1.66 g m-nitrobenzoyl peroxide (activity 98%), 50 ml ethylene glycol monoethyl ether and 50 g mercury were shaken and heated at the boiling point of the solvent for 6 hours. At the end of the reaction, the mercury was separated from the transparent solution. The latter gave a reaction for aldehyde. No mercury compounds were detected.

SUMMARY

1. Acetyl peroxide in benzene solution reacts at room temperature with metallic mercury with formation of mercurous acetate.

2. Chloroacetyl peroxide in benzene solution reacts with metallic mercury with or without heating with formation of mercurous chloroacetate.

3. Benzoyl peroxide in carbon tetrachloride or dioxane solution at room temperature reacts with metallic mercury to form mercurous benzoate.

4. Benzoyl peroxide in benzene solution in presence of hydroquinone does not react with metallic mercury.

5. m-Nitrobenzoyl peroxide in benzene and carbon tetrachloride in presence of mercury forms, with or without heating, only mercurous m-nitrobenzoate.

6. m-Nitrobenzoyl peroxide does not react with mercury in ethylene glycol monoethyl ether solution.

LITERATURE CITED

[1] G. A. Razuvaev, Yu. A. Oldekop and L. N. Grobov, J. Gen. Chem. 23, 589 (1953.)*

[2] G. A. Razuvaev, Yu. A. Oldekop and L. N. Grobov, Proc. Acad. Sci. USSR, 88, 77 (1953).

[3] G. A. Razuvaev, Sci. Memoirs Gorky State Univ. 15, 81 (1949).

[4] L. Vanino and E. Uhlfelder, Ber. 33, 1043 (1900).

[5] H. Gelissen and P. H. Hermans, Ber. 58, 285 (1925).

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Gorky State University

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*Original Russian pagination. See C.B. Translation.

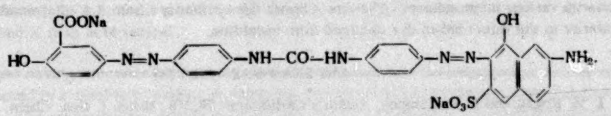
SYNTHESIS OF AZO DYES BASED ON 4,4'-DIAMINODIPHENYLUREA

D. F. Kutepov and Z. G. Vukolova

At the present time a large number of azo dyes are obtained on the basis of benzidine. The latter possesses carcinogenic properties; consequently its replacement in the manufacture of dyes by other intermediates is extremely desirable.

In our studies [1] we described a method for the preparation of 4,4'-dinitrodiphenylurea. The obtained 4,4'-dinitrodiphenylurea was reduced with iron (cast-iron shavings) [2]; The separation of the formed 4,4'-diaminodiphenylurea was effected by extraction with hot water, weak hydrochloric acid, and with the aid of organic flotation agents (butanol, isobutanol, ethyl alcohol and solvent). The flotation method using butanol gave the best results. With this method a product with a 92% amine content was obtained in a total yield of 98.2%. The concentration of the diamine in the butanol layer was a total of only 0.1%.

4,4'-Diaminodiphenylurea was subjected to diazotization and azo-coupling with 1,8-aminonaphthol-3,6-disulfonic acid (H-acid), m-phenylenediamine, 2,8-aminonaphthol-6-sulfonic acid (γ-acid), phenol, 2,5-aminonaphthol-7-sulfonic acid (J-acid), p-nitroaniline, salicylic acid and sulfanilic acid. Here we obtained a number of dyes with brown hues. Good results when tested were shown by the direct brown dye obtained in the azo-coupling of 4,4'-diaminodiphenylurea with 2,8-aminonaphthol-6-sulfonic acid and salicylic acid:



The new dye obtained in this manner proved to have a better fastness than the direct brown, obtained by the azo-coupling of benzidine with γ-acid and salicylic acid.

EXPERIMENTAL

Reduction of 4,4'-Dinitrodiphenylurea to the Diamine. A mixture of 20 g of purified iron shavings, 50 ml of water and 8 ml of concentrated hydrochloric acid was heated to the boil with stirring and then boiled for 10 minutes. After this 10 ml of butanol was added, and then 5 g of 4,4'-dinitrodiphenylurea. Since the dinitro product mixes poorly with water, it was charged as a paste, previously prepared from 5 g of the dinitro product and 50 ml of water; the paste was added in 5 minutes. The mixture was heated to 90° and kept at this temperature for 5 hours. The iron salts were precipitated with calcined soda (test with Na_2S). The diamine found in the sludge is very difficultly soluble in water and in organic solvents, and dissolves in hydrochloric acid only when heated; in this connection its isolation from the iron sludge presented some difficulties.

Isolation of 4,4'-Diaminodiphenylurea From Iron Sludge. a) Extraction with hot water. A mixture of the sludge, obtained from one experiment, and 100 ml of water was boiled with stirring for 30 minutes, and then it was filtered hot. White crystals with a grayish tinge deposited from the filtrate on cooling, which sublimed without melting when heated. After 10 extractions with hot water we obtained 0.85 g (21.2%) of 4,4'-diaminodiphenylurea.

Found %: C 64.09, 64.28; H 5.67, 5.94; N 23.09, 23.02. $C_{13}H_{14}ON_4$. Calculated %: C: 64.44; H 5.83; N 23.13.

b) Isolation with hydrochloric acid. The experiment was performed in the same manner as the preceding. The precipitate on the funnel after filtering was washed with hot dilute hydrochloric acid. The filtrate after cooling was made alkaline with calcined soda; the resulting precipitate was filtered and dried. We obtained 9.6 g of dry product with a 4,4'-diaminodiphenylurea content of 24.2% (53%, based on the dinitrodiphenylurea). The low diamine concentration in the product is explained by the large amount of impurities present, chiefly iron salts.

c) Isolation with the aid of organic flotation agents. A mixture of the sludge from one experiment, containing the diamine, 150 ml of water and 100 ml of butanol was stirred for 30 minutes at 25°, and just prior to the end of stirring was added 25 g of common salt. On conclusion of stirring the mixture was transferred to a cylinder for settling – separation of the butanol layer. The iron sludge quickly settled to the bottom of the cylinder. After separation, the butanol layer, containing the diamine as crystals, was filtered. The yield of dry product with a 92% content of 4,4'-diaminodiphenylurea was 4.82 g, which corresponds to a 98.2% yield.

The diazotization of the 4,4'-diaminodiphenylurea and its azo-coupling with the above indicated intermediates was run by known methods, already described in the literature [3].

SUMMARY

1. A method was developed for the isolation of 4,4'-diaminodiphenylurea from iron sludge in 98.2% yield by the flotation technique employing butanol.

2. In principle it was shown that it is possible to obtain azo dyes by the azo-coupling of 4,4'-diaminodiphenylurea with various intermediates. The direct brown dye synthesized from 4,4'-diaminodiphenylurea is in no way inferior to the direct brown dye obtained from benzidine.

LITERATURE CITED

[1] I. M. Kogan and D. F. Kutepov, Author's Certificate 78,379 (1949); J. Gen. Chem. 21, 1297 (1951) (T. p. 1419). *

[2] N. N. Vorozhtsov, Principles of the Synthesis of Intermediates and Dyes (1950), p. 261. **

[3] N. N. Vorozhtsov, Principles of the Synthesis of Intermediates and Dyes (1950), pp. 460, 475. **

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* T. p. = C. B. Translation pagination.

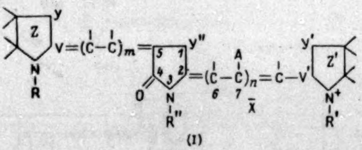
** In Russian.

CYANINE DYES

X. SOME MEROCYANINOCARBOCYANINES

M. V. Deichmeister, I. I. Levkoev and E. B. Lifshits

In recent years various polymethine dyes, containing several different chromophore systems, frequently conjugated with each other, have been described in the literature, mainly in the patent literature. Of these dyes the merocyaninocyanines, the derivatives of thia-, oxa, selena- and imidazolin-4-one of structure (I), and also of thiazolin-5-one, possess the greatest importance.



(I)

Where Y and Y' = O,S, Se, CH=CH, C$(CH_3)_2$, etc., V and V' = C or CH=CH (in the last case the groupings Y and Y' are absent); Y" = S, Se, O or NR; A = H, alkyl or another substituent; R, R' and R" are alkyls; m and n = 0, 1 or 2; and X is an acid radical.

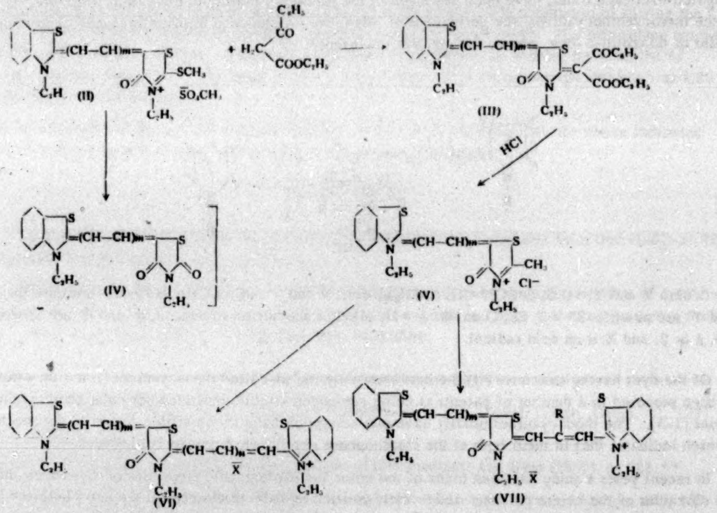
Of the dyes having structures (I) the best known are the so-called rhodacyanines (I; n = 0), which have been proposed in a number of patents as being component-stable sensitizers for color photographic material [1-5]. The rhodacyanines usually have one absorption band in the visible region of the spectrum [6], which indicates that in them both of the chromophore systems show mutual conjugation.

In recent years a study has been made of the color and photographic properties of these dyes, differing in the character of the hetero portions and in their position relative to the central nucleus [7-9] (see [5]). The vinylene homologs of the rhodacyanines – the merocarbo – and polycarbocyanines (I; n = 1, 2 or 3) – have been studied to a much lesser degree. Only several such dyes (n = 1), with an unsubstituted polymethine chain [10, 11], with an alkoxy [12-15], methylmercapto- [11, 13] or methyl group [11, 16] in the 7 position, and also the 6,8-trimethylene derivatives [17], have been briefly described.

In review [16] it is mentioned that the presence of a methyl, and especially of a methoxy group, in the 7 position of zero-methinethiamerocyaninocarbocyanines causes a shift of the absorption maximum of the dyes toward the short-wave region.

It seemed of interest to make a more detailed study of the properties of the merocyaninocarbocyanines, and in particular, to study the influence of lengthening the external chain in the merocyanine and cyanine portions of the molecule, the nature of the heterocyclic nitrogen portions and the presence of substituents in the 7 position of the polymethine chain on their color. In this connection we synthesized a number of zero- and dimethinemerocyaninocarbocyanine derivatives (I; n = 1; m = 0 or 1) of thiazolin-4-one (I; Y" = S), containing in the merocyanine portion of the molecule the benzothiazole and 4-quinoline portions and in the cyanine portion the benzothiazole, benzoxazole, 3,3-dimethylindolenine, 2-pyridine and 4,5-diphenylthiazole portions.*

The chain-unsubstituted zero- and dimethinemerocyaninocarbocyanines (for example VI; $n = 1$; $m = 0$ or 1) were obtained by the condensation of the alkiodides of the 2-β-acetanilinovinyl derivatives of benzothiazole, benzoxazole, 3,3-dimethylindolenine and 2-pyridine with the quaternary salts of the merocyanine derivatives of 2-methylthiazolin-4-one (V). These salts also readily react with 1,3,3-trimethyl-2-formylmethyleneindoline and the ethiodide of 2-β-methylmercaptovinyl-4,5-diphenylthiazole, and also with the ethiodide of 2-δ-acetanilinobutadienylbenzothiazole to form the merocyaninodicarbocyanine (VI; $n = 2$; $m = 0$), (see [10]). However, in a number of cases the formation of secondary saltlike dyes (mainly of the corresponding symmetrical carbocyanines) was observed here, which we were able to separate by chromatographing the reaction products on aluminum oxide. The condensation of the quaternary salts of the merocyanine derivatives of 2-methylthiazolin-4-one with the quaternary salts of the 2-alkylmercaptoalkenylbenzothiazoles also gave zero- and dimethinemerocyaninocarbocyanines, containing either the methyl or ethyl group in the 7 position, for example (VII):



The starting quaternary salts of the merocyanines with a methyl group in the 2 position, for example (V), were obtained by heating the dimerocyanine derivatives of 2-benzoylcarbethoxymethylene-3-ethylthiazolidin-4-one, for example (III), with hydrochloric acid. To synthesize the latter the quaternary salts of the merocyanine derivatives of 2-methylmercaptothiazolin-4-one (II) [18, 19] were condensed with ethyl benzoylacetate in anhydrous alcohol in the presence of triethylamine. This condensation proceeds quite smoothly, and the yields of pure dimerocyanines of the (III) type were 50-60% of the theoretical.

The condensation of the quaternary salts (II) with ethyl acetoacetate [10, 11] proceeds, as was revealed, much less satisfactorily. In the case of the dimethinemerocyanines, together with the derivatives of 2-acetylcarbethoxymethylenethiazolidin-4-one (30-40% yield), substantial amounts of the dyes with a thiazolidin-2,4-dione part (IV) were formed here, being the hydrolysis products of the original quaternary salt (II) [19-21]; the separation of these was easily achieved by chromatographing on aluminum oxide.

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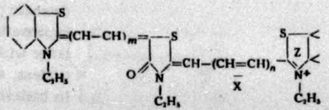
*Here the dyes are named in accord with the nomenclature used earlier for the rhodacyanines [7, 8].

The dimerocyanines (III) when heated with acids are quite easily hydrolyzed with the cleavage of benzoic and carbonic acids. In their properties the resulting quaternary salts of the merocyanine derivatives of 2-methylthiazolin-4-one (V) are extremely reminiscent of the quaternary salts of the 2-methyl derivatives of the simpler heterocyclic nitrogen bases. However, they are readily hydrolyzed in aqueous solutions, in which connection, the solutions become colorless and precipitates of the methylene bases separate, which when acidified again dissolve with restoration of the original color. The dimethine derivative (V; m = 1) is hydrolyzed with especial ease, as a result of which its recrystallization from anhydrous ethyl alcohol is expedient only in the presence of acid.

An SF-4 spectrophotometer was used to measure the absorption spectra of the synthesized dyes in $1 \cdot 10^{-4}$ M alcohol solutions. In the absorption spectra of the investigated merocyaninocyanines, in addition to the main band in the visible region, a quite intense shorter wave band is observed (depending on the length of the polymethine chain, with a maximum at 345-420 mμ). The presence of an additional absorption band was observed earlier for the simpler cyanine dyes [22]. However, for the merocyanines its intensity is considerably greater. The absorption curves for the merocyaninocyanines with a variable chain length in the cyanine and merocyanine portions of the molecule are shown in Figs. 1-3, while the positions of the absorption maxima of these dyes are given in Table 1. As can be seen from the Figures, in all cases a lengthening of the polymethine chain causes both absorption bands to shift toward longer waves, in which connection the main band becomes somewhat broader. The data in Table 1 show that a lenthening of the polymethine chain in the cyanine portion of the investigated dyes causes a bathochromic shift of their main absorption maximum, in magnitude completely analogous to that observed in the ordinary cyanine series. However, it should be mentioned that in the case of the dye with a benzothiazole part, a lesser deepening of the color is observed when a second vinylene group is introduced (a shift of 87 as against 131 mμ).

TABLE 1



Hetero nitrogen portion Z	m = n = 0 (Ia)	m = 0; n = 1 (IIa)	Shift (in mμ) (Ia) → (IIa)	m = 0; n = 2 (IIIa)	Shift (in mμ) (IIa) → (IIIa)	m = 1; n = 0 (IVa)	Shift (in mμ) (Ia) → (IVa)	m = n = 1 (Va)	Shift (in mμ) (IIa) → (Va)
	λmax. (in mμ)			λmax. (in mμ)		λmax. (in mμ)		λmax. (in mμ)	
Benzothiazole	345, 502	368, 633 *	23, 131	392, 720	24, 87	380, 600 [7]	35, 98	422, 696	54, 63
4,5-Diphenylthiazole	350, 500	376, 625	26, 125	— —	— —	384, 590 **	34, 90	423, 672	47, 47

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* According to the data of [6], λ max. = 635 mμ.

** We wish to thank Z. P. Sytnik, who was kind enough to furnish us the value of the absorption maximum of this dye.

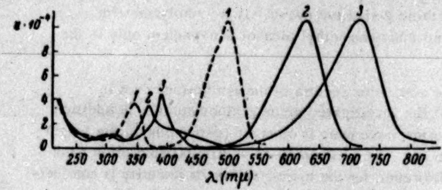


Figure 1. Absorption curves in ethyl alcohol of the merocyaninocyanines (I), Z = Z' = benzothiazole part.
1 – m = n = 0; 2 – m = 0, n = 1; 3 – m = 0, n = 2.

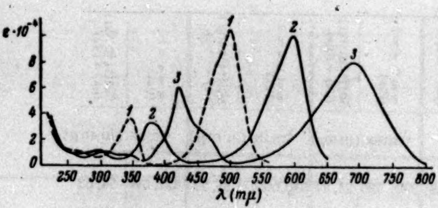


Figure 2. Absorption curves in ethyl alcohol of the merocyaninocyanines (I), Z = Z'=benzothiazole part.
1 – m = n = 0; 2 – m = 1, n = 0; 3 – m = n = 1.

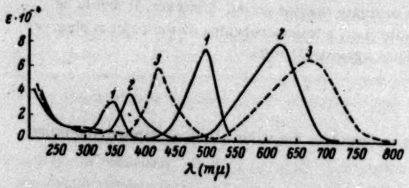


Figure 3. Absorption curves in ethyl alcohol of the merocyaninocyanines (I), Z = benzothiazole part, Z'=4,5-diphenylthiazole part.
1 – m = n = 0; 2 – m = 0, n = 1; 3 – m = n = 1.

A much smaller bathochromic shift of the absorption maximum in the transition from the mono- to the trimethine derivatives also occurs for the dyes with a dimethine chain in the merocyanine portion of the molecule.

Evidently, these facts are associated with the fact that the investigated merocyaninocyanines represent unsymmetrical polymethine dyes, for which, as is known, a bathochromic shift of the absorption maximum with elongation of the polymethine chain gradually decreases [23, 24] as the result of an increase in the nonuninformity of electron density distribution in the polymethine chromophore. With elongation of the chain in the merocyanine portion of the investigated compounds the electron shifts from the nitrogen of the heterocyclic part to the oxygen atom of the carbonyl group also decrease [24-27], which should lead to an increase in the electron reactivity of the latter with the nitrogen atom of the central nucleus, and consequently, to a reduction in its basicity. As a result, when compared with the zero-methine derivatives the dimethinemerocyaninocyanines are more asymmetrical compounds, in association with which a lesser bathochromic shift of the absorption maximum is observed for these dyes in the transition from the mono- to the trimethinecyanines.

It should be mentioned that a considerably greater deepening of the color is observed for the merocyaninomonomethinecyanines when the external chain in the merocyanine portion of the molecule is lengthened (for the thia derivatives a shift of 98 as compared to 63 m μ). This phenomenon is also associated with the fact that the corresponding carbocyanines are more asymmetrical due to a decrease in the basicity of the central nucleus and an increase in the electron shifts from the nitrogen atom of the latter to the oxygen atom of the carbonyl group, as a result of which the polarity of the merocyanine portion of the molecule and the uniformity of the electron density distribution in it show a decrease. From this viewpoint it appears logical for the absorption maxima of the dimethinemerocyaninocarbocyanines (I; m= n =1) to be situated in the shorter wave region when compared with those calculated on the basis of the vinylene shifts, observed in the transition from the zero-methinemerocyaninocyanines to the corresponding dimethine derivatives, on the one hand, and to the zero-methinemerocyaninocarbocyanines, on the other. These deviations for the dyes with benzothiazole and 4,5-diphenylthiazole parts are 37 and 43 mμ respectively.

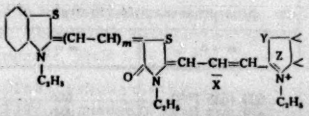
As was already mentioned above, the short-wave absorption band of the investigated dyes is also shifted toward the long-wave region when the chain is lengthened. The magnitude of this bathochromic shift in the case of the zero-methine derivatives is 23-26 mμ (see [22]), i. e, it is considerably less than the shift of the main band. In the case of the dimethine derivatives this shift is considerably greater (34-35 mμ), and with elongation of the chain in the cyanine portion of the molecule it increases even more (up to 47-54 mμ), whereas here the magnitude of the shift for the main band shows a decrease.

It was shown earlier [7] that the absorption maximum in the case of the rhodacyanines is shifted toward the short-wave region when the basicity of the hetero part in the cyanine portion of the dye molecule is increased, whereas a similar change in the basicity of the part in the merocyanine portion conditions a deepening of the color. It could be expected that the same rules would also apply to the investigated dyes.

In Table 2 we present the absorption maxima for a number of zero- and dimethinemerocyaninocarbocyanines, containing parts of different basicity in the cyanine portion of the molecule.

TABLE 2

Heterocyclic Nitrogen Portion Z



Heterocyclic nitrogen portion Z	$m = 0$	$m = 1$	Shift (in mμ)
	λmax. (in mμ)		
3,3-Dimethylindolenine	636	713	77
Benzothiazole	633	696	63
4,5-Diphenylthiazole	625	672	47

From the data in Table 2 it can be seen that in the transition from dyes with the weakly basic indolenine part to the thia- and 4,5-diphenylthiazole derivatives a hypsochromic shift of the absorption maximum is observed, which, evidently, is conditioned by a difference increase in the basicity of the right and central hetero portions, and as a result of this, an increase in the nonuniformity of electron density distribution in the dye chromophores (see [7]). In the transition from zero- to dimethine derivatives the vinylene shifts become smaller the more basic the hetero portion being changed, i.e., the greater the asymmetry of the dye molecule.

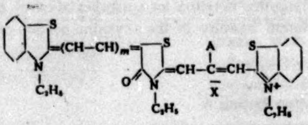
The absorption maxima for the 7-alkyl-substituted zero-and dimethinethiamerocyaninocarbocyanines are presented in Table 3. The introduction of a methyl group in the meso-position of the zero-methine derivative conditions a hypsochromic shift of the absorption maximum by 24 mμ (according to A. van Dormael, 22 mμ [16]). When the methyl group is replaced by ethyl this shift decreases to 19 mμ.

In the case of the dimethinethiamerocyaninocarbocyanine the hypsochromic shift of the absorption maximum is reduced to 10 mμ when a methyl group is introduced in the 7 position. As a result, the influence of introducing a methyl group in the meso-position on the color of the investigated dyes fails to differ in character from that observed in the tricarbocyanine series [28, 29] (see [16]).

The absorption maxima of the synthesized dimerocyanine derivatives of the 2-acetyl- and 2-benzoylcarbethoxymethylenethiazolidin-4-ones, and also of the original merocyanines with a rhodanine portion, are presented in Table 4.

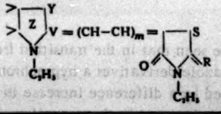
As can be seen from the presented data, replacement of the sulfur atom in the 2 position of the thiazolidin-4-one portion by the benzoylcarboethoxymethylene group in the case of the dyes with a benzothiazole part causes some heightening of the color, while for the merocyanines with 4-quinoline parts a substantial bathochromic shift of the absorption maximum is observed (by 7 mμ). The absorption maxima of the investigated merocyanine derivatives of 2-acetylcarbethoxymethylene-3-ethylthiazolidin-4-one are situated in the somewhat longer-wave region when compared with the derivatives of 3-ethylrhodanine and 2-benzoylcarbethoxymethylene-3-ethylthiazolidin-4-one. 4

TABLE 3



Value of A	Absorption maxima (in mμ)	
	m = 0	*m* = 1
H	633 (635 [10])	696
CH_3	612 (613 [10])	686
C_2H_5	617	—

TABLE 4



Value of R	λmax. (in mμ)		
	heterocyclic nitrogen portion Z		
	benzothiazole		4-quinoline
	m = 0	*m* = 1	*m* = 0
S	426	524	516
$=C\genfrac{}{}{0pt}{}{COC_6H_5}{COOC_2H_5}$	415	520	533
$=C\genfrac{}{}{0pt}{}{COCH_3}{COOC_2H_5}$	441	534	—

EXPERIMENTAL

3-Ethyl-5-(3'-ethylbenzothiazolin-2'-ylidene) thiazolidin-2-thion-4-one [30]. A mixture of 3.37 g of 2-methylmercaptobenzothiazole ethiodide, 1.6 g of 3-ethylrhodanine, 50 ml of anhydrous ethyl alcohol and 1 g of triethylamine was boiled for 30 minutes in a flask under reflux. The precipitated dye after cooling was filtered and washed with water and alcohol. Yield 2.56 g (80.7%). Yellow needles with m. p. 256-257°. The product was purified by washing with boiling ethyl alcohol (twice with 25 ml portions), after which it was used for the synthesis of the dyes. Weight 2.3 g.

3- Ethyl-5-(1'-ethyldihydroquinol-4'-ylidene) thiazolidin-2-thion-4-one [31]. To a solution of 0.23 g of metallic sodium in 25 ml of absolute ethyl alcohol was added 0.8 g of 3-ethylrhodanine and 2.85 g of quinoline ethiodide, and the mixture boiled for 10 minutes. The precipitated dye was filtered and washed with water and alcohol. Yield 0.75 g (47.4%). The product was purified by recrystallization from ethyl alcohol (1 g from 350 ml). Weight 0.7 g. Red needles with m. p. 200-201° (204-206° [31]).

Found %: C 60.66, 60.50; H 5.17, 5.18. $C_{16}H_{16}ON_2S_2$. Calculated %: C 60.72; H 5.09.

2-Methylmercapto-5-(1'-ethyldihydroquinol-4'-ylidene)-thiazolin-4-one Ethyl Perchlorate. A mixture of 1.2 g of 3-ethyl-5-(1'-ethyldihydroquinol-4'-ylidene) thiazolidin-2-thion-4-one and 1.5 g of dimethyl sulfate was heated for 10 minutes at 110-115° in a wide open test tube with manual stirring. The reaction mixture was washed by rubbing it with absolute ether (twice with 10 ml portions), the tarry mass was dissolved in 35 ml of dry methanol, and the solution was poured into 35 ml of 25% methanolic sodium perchlorate solution. The resulting precipitate was filtered, washed with dry methanol and ether, and then dried in a vacuum-desiccator. Yield 1.7 g (98.8%). Orange silky needles with m. p. 127° .

3-Ethyl-2-acetylcarbethoxymethylene-5-(3'-ethylbenzothiazolin-2'-ylidene) thiazolidin-4-one [11]. A mixture of 1.6 g of 3-ethyl-5-(3'-ethylbenzothiazolin-2'-ylidene) thiazolidin-2-thion-4-one and 1.89 g of dimethyl sulfate was heated for 15 minutes at 130°. After washing with absolute ether (twice with 30 ml portions) the residue was treated with 1.9 g of ethyl acetoacetate, 35 ml of anhydrous ethyl alcohol and 0.5 g of triethylamine, and the mixture was boiled in a flask under reflux for 30 minutes. The separated precipitate after cooling was filtered, and washed with water and alcohol. Weight 1.45 g; m. p. 156-158°. The yield after two recrystallizations from benzene (1 g from 13 ml) was 0.9 g (43%). Yellow prisms with m. p. 186-187° (226-229° [11]). Further purification failed to change the melting point. Readily soluble in benzene, and somewhat more difficultly soluble in ethyl alcohol.

Found %: N 6.54. $C_{20}H_{22}O_4N_2S_2$. Calculated %: N 6.68.

3-Ethyl-2-benzoylcarbethoxymethylene-5-(3'-ethylbenzothiazolin-2'-ylidene) thiazolidin -4-one (III; m = 0). A mixture of 0.16 g of 3-ethyl-5-(3-ethylbenzothiazolin-2'-ylidene) thiazolidin-2-thion-4-one and 0.19 g of dimethyl sulfate was heated at 130° for 15 minutes. After washing with absolute ether (twice with 20 ml portions) the residue was treated with 0.19 g of ethyl benzoylacetate, 5 ml of anhydrous ethyl alcohol and 0.05 g of triethylamine, and the mixture was boiled in a flask under reflux for 30 minutes. The separated precipitate after cooling was filtered and washed with water and alcohol. Yield 0.14 g (57.8%); m. p. 232-234°. After two recrystallizations from ethyl alcohol (1 g from 50 ml) the weight was 0.08 g (33%). Yellow needles with m. p. 245-247°. Quite readily soluble in benzene, and somewhat more difficultly soluble in ethyl alcohol.

Found %: N 5.12. $C_{25}H_{24}O_4N_2S_2$. Calculated %: N 5.00.

3-Ethyl-2-acetylcarbethoxymethylene-5-(3'-ethylbenzothiazolin-2'-ylidene-ethylidene) thiazolidin-4-one. A mixture of 0.34 g of 3-ethyl-5-3'-ethylbenzothiazolin-2'-ylidene-ethylidene)-thiazolidin-2-thion-4-one and 0.38 g of dimethyl sulfate was heated for 15 minutes at 130°. The product was washed with absolute ether (3 times with 10 ml portions), then treated with 0.39 g of ethyl acetoacetate, 20 ml of anhydrous ethyl alcohol and 0.11 g of triethylamine, and the mixture boiled for 1 hour in a flask under reflux. The precipitate that began to separate even during the heating was filtered, and washed with water and alcohol. Weight 0.23 g; m. p. 186-187°. For purification a benzene solution of the dye was chromatographed on aluminum oxide; here the yellow by-product was easily separated, and the reddish-violet substance was absorbed on the aluminum oxide. The latter, after complete removal of the yellow product by washing with benzene, was desorbed with chloroform. After removal of the chloroform by evaporation in vacuo the residue was recrystallized from ethyl alcohol (1 g from 360 ml). Yield 0.17 g (38.2%). Tiny red needles with m. p. 222°. It showed maximum absorption in ethyl alcohol at 534 mμ.

Found %: N 6.20. $C_{22}H_{24}O_4N_2S_2$. Calculated %: N 6.30.

From the benzene solution we isolated 0.2 g of yellow plates with m. p. 221° which failed to depress the melting point when mixed with 3-ethyl-5-(3'-ethylbenzothiazolin-2'-ylidene-ethylidene)thiazolidin-2,4-dione.

3-Ethyl-2-benzoylcarbethoxymethylene-5-(3'-ethylbenzothiazolin-2'-ylidene-ethylidene) thiazolidin-4-one (III; m = 1). A mixture of 2.45 g of 2-methylmercapto-5-(3'-ethylbenzothiazolin-2'-ylideneethylidene) thiazolin-4-one ethiodide, 1.9 g of ethyl benzoylacetate, 7.5 ml of anhydrous ethyl alcohol and 0.5 g of triethylamine was boiled for 30 minutes in a flask under reflux. After 6 hours the precipitate, already separating out during reaction, was filtered and washed with water and alcohol. Yield 1.56 g (65%); m. p. 219-221°. After two recrystallizations from ethyl alcohol (1 g from 30 ml) the weight was 1.25 g. Red prisms with m. p. 225°.

Found %: N 5.50. $C_{27}H_{26}O_4N_2S_2$. Calculated %: N 5.53.

3-Ethyl-2-benzoylcarbethoxymethylene-5-(1'-ethyldihydroquinol-4'-ylidene) thiazolidin-4-one. A mixture of 0.86 g of 2-methylmercapto-5-(1'-ethyldihydroquinol-4'-ylidene) thiazolin-4-one ethyl perchlorate, 0.77 g of ethyl benzoylacetate, 20 ml of anhydrous ethyl alcohol and 0.2 g of triethylamine was boiled for 30 minutes in a flask under reflux. The resulting precipitate was filtered and washed with water and alcohol. Yield 0.64 g (67.5%); m. p. 153-154°. After two recrystallizations from ethyl alcohol (1 g from 33 ml) the weight was 0.55 g. Red plates with m. p. 153-154°.

Found %: N 6.11. $C_{27}H_{26}O_4N_2S$. Calculated %: N 5.90.

2-Methyl-5-(3'-ethylbenzothiazolin-2'-ylidene) thiazolin-4-one Ethochloride and Ethiodide [11] (V; m = 0). A mixture of 0.418 g of 3-ethyl-2-acetylcarbethoxymethylene-5-(3'-ethylbenzothiazolin-2'-ylidene)thiazolidin-4-one and 8.8 ml of 25% hydrochloric acid was boiled for 30 minutes in a flask under reflux. The liquid was evaporated in vacuo to dryness, the residue washed with a small amount of dry acetone, dissolved in 5 ml of dry methanol, and the solution treated with absolute ether. The resulting precipitate was filtered and washed with absolute ether. Weight 0.27 g; m. p. 170°. For purification the product was washed with 10 ml of boiling anhydrous benzene. Yield 0.2 g (47.8%). Yellow needles with m. p. 200° (186-188° [11]).

A solution of 0.8 g of the ethochloride in 10 ml of anhydrous methanol was poured into 10 ml of a 10% methanolic solution of sodium iodide. The resulting precipitate was filtered and washed with anhydrous methanol and ether. Yield 0.82 g (80.6%); m. p. 209°. After two recrystallizations from anhydrous methanol (1 g from 70 ml) the weight was 0.57 g. Yellow prisms with m. p. 211-212° (217-220° [10], 198-199° [11]).

Found %: N 6.35, 6.39. $C_{15}H_{17}ON_2S_2I$. Calculated %: N 6.48.

2-Methyl-5-(3'-ethylbenzothiazolin-2'-ylideneethylidene)-thiazolin-4-one Ethiodide (V; m = 1). A solution of 2.38 g of 3-ethyl-2-benzoylcarbethoxymethylene-5-(3'-ethylbenzothiazolin-2'-ylideneethylidene) thiazolidin-4-one in 44 ml of 25% hydrochloric acid was boiled for 30 minutes in a flask under reflux. The liquid was evaporated in vacuo to dryness, the residue washed with absolute ether and anhydrous acetone, dissolved in 10 ml of anhydrous methanol, and treated with 10 ml of a 20% methanol solution of sodium iodide. The resulting precipitate was filtered and washed with dry methanol and ether. Weight 1.57 g; m. p. 182°. For purification the product was recrystallized three times from anhydrous methanol (1 g from 300 ml), containing hydriodic acid. Yield 1.03 g (45.8%). Dark red prisms with

m. p. 193° (199-201° [10]). Readily soluble in water, more difficultly soluble in ethyl alcohol and acetone, and practically insoluble in benzene. A water solution turns turbid and is decolorized almost immediately. Its absorption maximum in ethyl alcohol in the presence of hydrochloric acid is at 508 mμ.

Found %: N 5.24. $C_{17}H_{19}ON_2S_2I$. Calculated %: N 5.11.

2-Methyl-5-(1'-ethyldihydroquinol-4'-ylidene)thiazolin-4-one Ethiodide. A mixture of 0.47 g of 3-ethyl-2-benzoylcarbethoxymethylene-5-(1'-ethyldihydroquinol-4'-ylidene) thiazolidin-4-one and 10 ml of 16% hydrochloric acid was boiled for 30 minutes in a flask under reflux. The solution was evaporated in vacuo to dryness, the residue washed with absolute ether and acetone, dissolved in 4 ml of dilute hydrochloric acid (1:10), and treated with 0.2 g of potassium iodide. After 1 hour the obtained precipitate was filtered and washed with dilute hydrochloric acid. Yield 0.25 g (64.8%); m. p. 110°. After 2 recrystallizations from anhydrous ethyl alcohol (1 g from 13.5 ml), containing hydriodic acid, the weight was 0.16 g. Light-yellow prisms with m. p. 116°.

Found %: N 6.37. $C_{17}H_{19}ON_2SI$. Calculated %: N 6.57.

Merocyaninocarbocyanines. The preparation conditions, yields, melting points and analysis results for the merocyaninocarbocyanines are given in Table 5, where the following designations were adopted for the starting products: 2-methyl-5-(3'-ethylbenzothiazolin-2'-ylidene)thiazolin-4-one ethochloride (No. 1), 2-methyl-5-(1'-ethyldihydroquinol-4'-ylidene) thiazolin-4-one ethiodide (No. 2), 2-methyl-5-(3'-ethylbenzothiazolin-2'-ylideneethylidene) thiazolin-4-one ethiodide (No. 3), 2-β-acetanilinovinyl-benzothiazole ethiodide (No. 4), 2-β-acetanilinovinyl-benzoxazole ethiodide (no. 5), 1,3,3-trimethyl-2-formylmethyleneindoline (No. 6), 2-β-acetanilinovinylpyridine ethiodide (No. 7), 2-β-methylmercapto-vinyl-4,5-diphenylthiazole ethiodide (No. 8), 3,3-dimethyl-2-β-acetanilinovinylindolenine methiodide (No. 9), 2-β-methylmercaptopropenylbenzothiazole ethyl methyl sulfate (No. 10), 2-β-methylmercapto-butenylbenzothiazole ethyl p-toluenesulfonate (No. 11).

In all cases the isolated dyes after filtration were washed with water and ethyl alcohol, and then recrystallized to a constant melting point. In some cases the reaction products were first chromatographed on aluminum oxide.

3,3'-Diethyl-4-keto-5-(3"-ethylbenzothiazolin-2"-ylidene)-thiazolinothiacyanine Bromide (VI; m = n = 0). A mixture of 0.32 g of 3-ethyl-5-(3'-ethylbenzothiazolin-2'-ylidene)-thiazolidin-2-thion-4-one and 0.38 g of dimethyl sulfate was heated for 15 minutes at 130° (inside the mixture). After washing with absolute ether the residue was treated with 1.05 g of 2-methylbenzothiazole ethyl p-toluenesulfonate and 5 ml of pyridine and the mixture was boiled for 1 hour in a flask under reflux. After cooling 200 ml of ether was added, which was decanted the next day, the residue was dissolved in 25 ml of boiling ethyl alcohol, and the obtained solution was poured into 75 ml of a 10% water solution of potassium bromide. The dye that separated here was filtered and washed with water, alcohol and ether. Yield 0.47 g (86%); m. p. 236-238°. For purification the dye was boiled with 30 ml of benzene, and then recrystallized twice from ethyl alcohol (1 g from 150 ml). Weight 0.35 g. Silky orange needles with m. p. 239-241°.

Found %: Br 14.49, 14.42. $C_{24}H_{24}ON_3S_3Br$. Calculated %: Br 14.62.

3,3'-Diethyl-4',5'-diphenyl-4-(3"-ethylbenzothiazolin-2"-ylidene) thiazolinothiazolocyanine Iodide. Obtained in the same manner as the preceding dye by heating a mixture of 0.32 g of 3-ethyl-5-(3'-ethylbenzothiazolin-2'-ylidene)thiazolidin-2-thion-4-one with 0.38 g of dimethyl sulfate and condensation of the obtained quaternary salt with 0.75 g of 2-methyl-4,5-diphenylthiazole ethyl p-toluenesulfonate in 3 ml of pyridine. Yield 0.65 g (98.5%), m. p. 187-189°. After washing with boiling benzene and 2 recrystallizations from ethyl alcohol (1 g from 130 ml) the weight was 0.58 g. Lustrous orange plates with m. p. 187-189°. Its absorption maximum in ethyl alcohol is found at 530 mμ.

Found %: I 18.55. $C_{32}H_{30}ON_3S_3I$. Calculated %: I 18.24.

TABLE 5

Name of dye	Starting substances (in g)	Solvent (in ml)	boiling time (in min)	Yield (in %)	Solvent for recrystallization (in ml per g of dye)	Appearance	Melting point	Absorption maximum (in μ)	Analysis		
									found N (%)	empirical formula	Calculated N (%)
3,3′-Diethyl-4-keto-5-(3″-ethylbenzothiazolin-2″-ylidene)-thiazolinothiacarbocyanine iodide [10] (VI: m=0, n=1)	No 1–0.17, No 4–0.22	Pyridine (5)	40	35.5	Ethanol (800)	Lustrous green needles	262–263* (287–288[10])	633 (635[16])	675	$C_{26}H_{26}ON_3S_3I$	678
3,3′-Diethyl-4-keto-5-(3″-ethylbenzothiazolin-2″-ylidene)-thiazolinooxacarbocyanine iodide	No 1–0.17 No 5–0.22	Pyridine (5)	25	26.5	Anhydrous ethanol (400)	Fine green needles	231	597	7.10	$C_{26}H_{26}O_2N_3S_2I$	6.96
3-Ethyl-1′,3′,3′-trimethyl-4-keto-5-(3″-ethylbenzothiazolin-2″-ylidene) thiazolinoindocarbocyanine iodide	No 1–0.17 No 6–0.11	Acetic anhydride (5)	30	58.5	Ethanol (30)	Green prisms	240–241	636	6.69	$C_{28}H_{30}ON_3S_2I$	6.82
3,1′-Diethyl-4-keto-5-(3″-ethylbenzothiazolin-2″-ylidene)-thiazolino-2-pyridocarbocyanine iodide*	No 1–0.17 No 7–0.20**	Anhydrous ethanol (10)	30	14.2	Ethanol (200)	Fine dark-red needles	185–187	572	7.18	$C_{24}H_{26}ON_3S_2I$	7.45
3,3′-Diethyl-4′,5′-diphenyl-4-keto-5-(3″-ethylbenzothiazolin-2″-ylidene) thiazolinothiazolocarbocyanine iodide	No 1–0.17, No 8–0.23	Pyridine (5)	40	55.5	Ethanol (375)	Brownish prisms with a bronze luster	228	625	5.64	$C_{34}H_{32}ON_3S_3I$	5.82
3,3′-Diethyl-4′,5′-diphenyl-4-keto-5-(1″-ethyldihydroquinol-4″-ylidene) thiazolinothiazolocarbocyanine perchlorate*	No 2–0.20 No 8–0.23	Pyridine (3)	30	24.7	Methanol (250)	Fine green prisms	263–264	650	Cl 5.20	$C_{35}H_{34}O_5N_3S_2Cl$	Cl 5.15

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* The dye prior to recrystallization was purified by chromatographing on aluminum oxide.

** 0.05 g of triethylamine was taken.

Continuation of Table 5

Name of dye	Starting substances (in g)	Solvent (in ml)	boiling time (in min)	Yield (in %)	Solvent for recrystallization (in ml per g of dye)	Appearance	Melting point	Absorption maximum (in μ)	Analysis		
									found N (%)	empirical formula	Calculated N (%)
3,3'-Diethyl-4-keto-5-(3''-ethylbenzothiazolin-2''-ylidene-ethylidene)thiazolinothiacarbocyanine iodide [10]* (VI; m = n = 1)	No 3–0.23, No 4–0.22	Pyridine (2.5)	20	27.9	Ethanol (1100)	Fine dark-brown needles	243-244° (273[10])	696	6.33	$C_{28}H_{28}ON_3S_3I$	6.50
3-Ethyl-1',3',3'-trimethyl-4-keto-5-(3''-ethylbenzothiazolin-2''-ylidene-ethylidene)thiazolinoindocarbocyanine iodide	No 3–0.23, No 9–0.22	Pyridine (5)	10	18.7	Benzene-ethyl alcohol (9 : 1) (500)	Brown prisms with a golden luster	260	713	6.53	$C_{30}H_{32}ON_3S_2I$	6.54
3,3'-Diethyl-4-keto-4',5'-diphenyl-5-(3''-ethylbenzothiazolin-2''-ylideneethylidene)thiazolinothiazolocarbocyanine iodide	No 3–0.23, No 8–0.23	Pyridine (5)	30	37.4	Ethanol (670)	Dark brown prisms	239	672	5.49	$C_{36}H_{34}ON_3S_3I$	5.61
3,3'-Diethyl-4-Keto-7-methyl-5-(3''ethylbenzothiazolin-2''-ylidene)thiazolinothiacarbocyanine iodide* (VII; m = 0; R = methyl)	No 1–0.17, No 10–0.18**	Anhydrous ethanol (15)	40	44.2	Ethanol (700)	Fine Dark-green needles	236-237	612 (613[16])	6.49	$C_{27}H_{28}ON_3S_3I$	6.63
3,3'-Diethyl-4-keto-7-ethyl-5-(3''-ethylbenzothiazolin-2''-ylidene)thiazolinothiacarbocyanine iodide* (VII; m = 0; R = ethyl)	No 1–0.34 No 11–0.44	Pyridine (3)	30	6.1	Ethanol (300)	Fine dark-blue needles	231-233	617	--	- - -	--
3,3'-Diethyl-4-keto-7-methyl-5-(3''-ethylbenzothiazolin-2''-ylidene)thiazolinothiacarbocyanine iodide (VII; m = 1; R = methyl)	No 3–0.23, No 10–0.18	Pyridine (5)	20	3.33	Ethanol (100	Dark-green needles with a bronze luster	237	686	6.51	$C_{29}H_{30}ON_3S_3I$	6.37

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* The dye prior to recrystallization was purified by chromatographing on aluminum oxide.

**0.3 g of triethylamine was taken.

3,3'-Diethyl-4-keto-5-(3''-ethylbenzothiazolin-2''-ylidene)-thiazolinothiadicarbocyanine iodide [10] (VI; m=0, n= 2.) A mixture of 0.21 g of 2-methyl-5-(3'-ethylbenzothiazolin-2'-ylidene) thiazolin-4-one ethiodide, 0.24 g of 2- δ -acetanilinobutadienylbenzothiazole ethiodide and 2 ml of pyridine was heated for 5 minutes at 130° in a flask under reflux. After 6 hours the dye, already separating from the hot solution, was filtered and washed with water, alcohol and ether. Weight 0.2 g; m. p. 231°. For purification the dye was fractionally crystallized from ethyl alcohol, in which connection the first fractions contained a by-product with m. p. 252° (the alcohol solution was colored blue). The subsequent fractions with m. p. 214-216° were combined and again recrystallized from ethyl alcohol (1 g from 1300 ml). Here the melting point did not change. Yield 0.07 g (21.7%); fine green needles with m. p. 214-216° (239-241° [10]). Its absorption maximum in ethyl alcohol was found at 720 mμ, and its sensitization maximum at 757 mμ.

Found %: N 6.45. $C_{28}H_{28}ON_3S_3I$. Calculated %: N 6.50.

SUMMARY

1. A number of chain-unsubstituted zero- and dimethinemerocyaninocarbocyanine derivatives of thiazolin-4-one were synthesized, differing in the nature of the terminal heterocyclic nitrogen portions, and also some similar dyes with benzothiazole portions, containing alkyl groups in the 7 position.

2. It was shown that in the absorption spectra of the merocyaninocyanines, in addition to the principal band in the visible region, there is also present a fairly intense band in the shorter wavelength portion of the spectra.

3. It was established that a lengthening of the polymethine chain in the cyanine portion, and especially in the merocyanine portion of the investigated dyes, leads to a substantial decrease in the bathochromic shift of the main absorption maximum. This phenomenon testifies to an increase in the asymmetry of the dye molecules.

4. It was shown that an increase in the basicity of the heterocyclic nitrogen portion in the cyanine portion of the merocyaninocarbocyanine molecules, the same as was true for the earlier studied rhodacyanines, results in a heightened color for the dyes.

5. The introduction of either a methyl or ethyl group in the 7 position of the zero- and dimethinethiamerocyaninocarbocyanines, the same as was true for the thiacarbocyanines, determines a hypsochromic shift of the absorption maximum.

LITERATURE CITED

[1] Brit. Patent 487,051, 489,335; Fr. Patent 82,903.

[2] Swiss Patent 218,381; Belg. Patent 449,126.

[3] U. S. Patent 2438782.

[4] U. S. Patent 2504468.

[5] E. B. Knott, R. A. Jeffreys, J. Chem. Soc., 1952, 4762.

[6] K. Miz, Theory of the Photographic Process,* (Techn.-Theoret. Lit. Press, 1949) p.746.

[7] I. I. Levkoev, Z. P. Sytnik and S. V. Natanson, Prog. Sci. Photography, 2, 11 (1955).

[8] E. B. Lifshits, Dissertation, Moscow (1951).

[9] E. B. Knott, J. Chem. Soc., 1955, 949.

[10] U. S. Patent 2263018.

[11] A. E. van Dormael, Bull. Soc. Chim. Belg., 57, 332, 364 (1948).

[12] N. N. Sveshnikov, I. I. Levkoev, A. F. Vompe and B. S. Portnaya, Proc. Acad. Sci. USSR, 88, 281 (1953); N. N. Sveshnikov, T. G. Gnevysheva, I. I. Levkoev and M. V. Deichmeister, Author's Certificate, USSR 93, 725.

---

* In Russian.

[13] Brit. Patent 646137.

[14] Brit. Patent 714276.

[15] A. E. van Dormael, J. Nys, Bull, Soc. Chim. Belg., 62, 199 (1953).

[16] A. E. van Dormael, Ind. Chim. Belg., 18, 1297 (1953).

[17] I. I. Levkoev, N. N. Sveshnikov and M. V. Deichmeister, Author's Certificate, USSR 93,611.

[18] Brit. Patent 505839, 509927; Brit. Patent 487051.

[19] Z. P. Sytnik, I. I. Levkoev and M. V. Deichmeister, J. Gen. Chem., 21, 768 (1951). (T. p. 847)*

[20] Z. P. Sytnik, M. V. Deichmeister, T. G. Gnevysheva and L. D. Zhilina, Author's Certificate, USSR 81,881.

[21] Z. P. Sytnik, I. I. Levkoev, M. V. Deichmeister and L. D. Zhilina, J. Gen. Chem., 22, 1228 (1952). (T. p. 1273)*

[22] A. I. Kiprianov and V. E. Petrunkin, J. Gen. Chem., 10, 620 (1940).

[23] L. G. S. Brooker, Rev. of mod. Phys., 14, 275 (1942).

[24] L. G. S. Brooker, Frontiers in Chemistry, III, 63 (1945).

[25] L. G. S. Brooker, G. H. Keyes, R. H. Sprague, R. H. van Dyke, E. van Lare, G. van Zandt, F. L. White, J. Am. Chem. Soc., 73, 5326 (1951).

[26] L. G. S. Brooker, G. H. Keyes, R. H. Sprague, R. H. van Dyke, E. van Lare, G. van Zandt, F. L. White, H. W. J. Cressman, S. G. Dent, J. Am. Chem. Soc., 73,5332 (1951).

[27] M. V. Deichmeister, I. I. Levkoev and E. B. Lifshits, J. Gen. Chem., 23, 1529 (1953).(T.p. 1601)*

[28] L. G. S. Brooker, F. L. White, J. Am. Chem. Soc., 57, 2480 (1935).

[29] A. I. Kiprianov, Z. P. Sytnik and E. D. Sych, J. Gen. Chem., 6, 42 (1936).

[30] Brit. Patent 462820.

[31] U. S. Patent 2185182.

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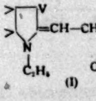
*T.p. = C.B. Translation pagination.

MEROCYANINE DYES OF RHODANINE DERIVATIVES

VII. THE REACTION PRODUCTS OF 3-ETHYL-5-(3'-ETHYL-6'-DIETHYLAMINOBENZOTHIAZOLIN-2'-YLIDENEETHYLIDENE)-THIAZOLIDIN-2-THION-4-ONE WITH DIMETHYL SULFATE AND THEIR TRANSFORMATIONS

Z. P. Sytnik and L. D. Zhilina

As a continuation of our studies of the quaternary salts of the dimethinemerocyanines of general structure (I) [1-2], we proposed to make a study of the properties of the compounds of this type in which polar substituents – the nitro or diethylamino group – were present in the 6 position of the benzothiazole portion (II).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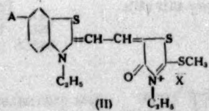
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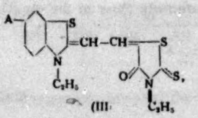
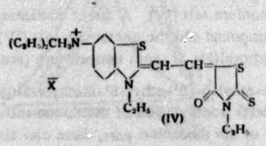
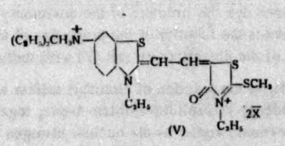

(III)

where: V = O, S, Se, CH=CH or $C(CH_3)_2$, A = NO_2 or $N(C_2H_5)_2$, X = acid radical

Dyes of structure (II) can be obtained by heating merocyanines (III) with excess dimethyl sulfate [1-3]. With this method the quaternary salt with a 6-nitrobenzothiazole part (II, A = NO_2) was synthesized with very little difficulty. However in the reaction of alkylation agents, in particular dimethyl sulfate, with 3-ethyl-5-(3'-ethyl-6'-diethylaminobenzothiazolin-2'-ylideneethylidene)thiazolidin-2-thion-4-one (III, A = $N(C_2H_5)_2$), together with the quaternary salt – the 6-diethylaminobenzothiazole derivative (II, A = $N(C_2H_5)_2$), the formation of the isomeric compound (IV) and of the diquaternary salt (V) could be expected as the result of one molecule of dimethyl sulfate reacting with the diethylamino group (see [4-6]):

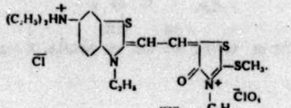

(IV)


(V)

When the above indicated merocyanine (III, $A = N(C_2H_5)_2$) was heated with 3 moles of dimethyl sulfate at 130-135° we obtained a product that was readily soluble in water and alcohol and insoluble in ether and benzene, which we isolated as the perchlorate. When the perchlorate was purified by fractional washing with absolute ethyl alcohol under heating it was observed that the color of the alcohol solutions increases, and the solubility of the dye falls sharply in this connection. The residue showed an absorption maximum at 539 mμ* (Fig. 1, Curve 3), and based on the chromatographic study data, represented an individual substance, tenaciously adsorbed on the aluminum oxide as a narrow purple ring.

In the adsorbed state this compound is extremely unstable and rapidly decomposes with the formation of a yellow substance (absorption maximum at 455 mμ). In contrast to the earlier described quaternary salts of the (I) type, the obtained dye failed to dissolve in chloroform. Its chemical analysis data agreed well with those calculated for the diquaternary salt (V).

A more deeply colored dye was isolated from the alcohol extracts by the chromatographic method, forming a dark-violet band on the aluminum oxide, situated below the zone of the diquaternary salt (V) and easily separated from the latter. The isolated dye also showed the character of a quaternary salt — readily soluble in water, moderately soluble in alcohol and chloroform, and insoluble in benzene and ether. Its alcohol solution gave a broad absorption band with an ill-defined maximum (at 557 mμ), characteristic for the polymethine dyes with an amino group in the heterocyclic portions [46]. When an alcohol solution of this compound was acidified the absorption band shifted toward shorter wavelengths, and in shape and the position of the maximum (538 mμ) it became comparable to the absorption curve for the diquarternary salt (V) (539 mμ) (Fig. 1). On the basis of the described properties it is evident that the obtained dye represents a quaternary salt with the 6-diethylamino-benzothiazole portion (II, $A=N(C_2H_5)_2$), which is confirmed by the results of its elementary analysis. An increase in the color and a change in the shape of the absorption band for this dye when acidified are fully in order, since here salt (VI) is formed (see, for example [7, 8]), in its structure extremely close to the diquarternary salt (V):



(VI)

We obtained the quaternary salt (II, $A= N(C_2H_5)_2$) in good yield by heating the merocyanine (III, $A=N(C_2H_5)_2$) with three moles of dimethyl sulfate under milder conditions — in toluene solution. Here as secondary reaction products we isolated in small amounts the diquaternary salt (V) and an orange dye, insoluble in chloroform, benzene and ether, and tenaciously adsorbed on aluminum oxide, which indicated its saltlike character. The absorption curves of this compound and of the acidified solution of the starting merocyanine (III, $A=N(C_2H_5)_2$) proved to be identical in shape and extremely close to each other in the position of their maximum (Fig. 2, Curves 2 and 3). These properties and the analysis results caused us to assign the obtained dye the structure of the quaternary ammonium salt (IV). A direct confirmation of the proposed structure is the identity of the properties of this compound and the quaternary salt (IV), obtained by the reaction of the diquarternary salt (V) with sodium hydrosulfide at room temperature (see [9]).

As a result, in the reaction of dimethyl sulfate with 3-ethyl-5-(3'-ethyl-6'-diethylaminobenzothiazolin-2'-ylidene)-thiazolidin-2-thion-4-one, together with methylation of the thiono sulfur and the formation of a cationic center at the nuclear nitrogen atom of the rhodanine part, there can also occur the addition of dimethyl sulfate to the diethylamino group. As a result of this a mixture of the quaternary (II, $A = N(C_2H_5)_2$) and diquarternary (V) salts is mainly formed, depending on the reaction conditions with a predominance of one of them. Here the quaternary ammonium salt (IV) is obtained in very small amount as an impurity. It is impossible to truthfully say that it is the product of the primary reaction of the above indicated merocyanine (III, A = N $(C_2H_5)_2$) with dimethyl sulfate at the diethylamino group. The possibility for the formation of this compound as the result of dealkylating the diquaternary salt (V) is not excluded (for example, see [10]).

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*The absorption curves of all of the described dyes were measured in ethyl alcohol using an SF-2 spectrophotometer. Anhydrous ethyl alcohol was used for the (II) quaternary salts.

The formation of a quaternary salt at an outer ring nitrogen atom has been observed in a number of cases involving the synthesis of the quaternary salts of amino-substituted heterocyclic bases [4-6].

In the process of purifying the ammonium salt (IV), obtained by the reaction of the diquaternary salt (V) with sodium hydrosulfide, we isolated a dye, which, in contrast to the main reaction product (IV), readily dissolved in benzene and other nonpolar solvents and was weakly adsorbed on aluminum oxide, i.e., it showed the typical properties of the nonsaltlike merocyanines. This led us to think that in a weakly alkaline medium the quarternary salt (IV) suffers partial dealkylation with the formation of a merocyanine of the (III) type with either a diethyl- or methylethylamino group:

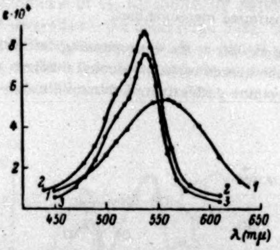


Figure 1. Absorption curves of the quaternary salts.

1 — [III, A = $N(C_2H_5)_2$, X = ClO_4], 2 — [III, A = $N(C_2H_5)_2$, X = ClO_4] + 250 moles HCl, 3 — (V, X = ClO_4).

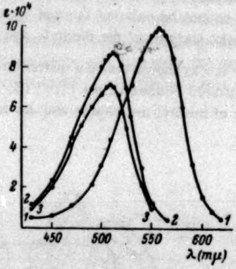


Figure 2. Absorption curves of the merocyanines.

1 — [III, A = $N(C_2H_5)_2$], 2 — [III, A = $N(C_2H_5)_2$] + 250 moles HCl, 3 — (IV, X = ClO_4).

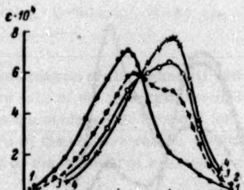


Figure 3. Absorption curves of merocyanine (IV) after heating in pyridine for various periods of time.

1–10 min., 2–40 min., 3–70 min., 4–100 min.

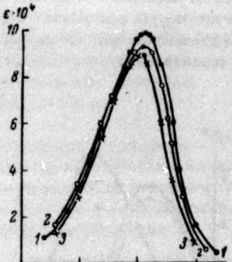
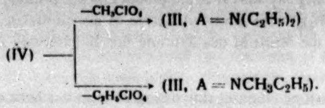


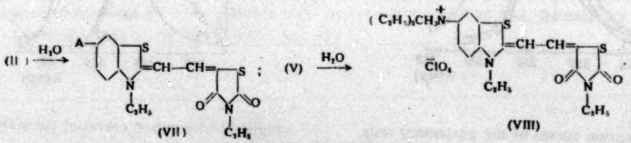
Figure 4. Absorption curves of merocyanines (III).

1 — A = $N(C_2H_5)_2$, 2 — A = $NCH_3C_2H_5$, 3 — A = $N(CH_3)_2$.



It was natural to expect that this reaction could be driven to completion by heating the ammonium salt (IV) with organic bases, for example, with pyridine. Actually, under these conditions a dye is formed in nearly quantitative yields, in its properties identical with the above described reaction product (Fig. 3). It remained obscure whether the obtained merocyanine, in accord with the presented scheme, contained the diethylamino or the methylethylamino group. The latter seems more probable, since the absorption maximum of the reaction product (555 mμ) lies between the absorption maxima of the diethyl- and dimethylamino derivatives (557 and 553 mμ [11], respectively, Fig. 4). Unfortunately, in this case the chemical analysis data cannot be enlisted as proof for the structure of the obtained compound due to the small difference in the molecular weights of the diethyl- and methylethylamino-substituted merocyanines.

Further it was shown that the quaternary salts of structure (II), as well as the corresponding derivatives of the unsubstituted benzothiazole [1, 2] (II, A = H), decompose when heated in water-alcohol medium with the evolution of methyl mercaptan and the formation of the merocyanine derivatives of thiazolidin-2,4-dione (VII):



Under similar conditions the decomposition of the diquaternary salt (V) also proceeds with the evolution of methyl mercaptan. However the substance formed here, similar to the starting product and the quaternary ammonium salt (IV), in insoluble in chloroform and is tenaciously adsorbed on aluminum oxide. The indicated properties and the close similarity of the absorption curves of this dye and the merocyanine (VII, A = $N(C_2H_5)_2$) in acid solution (Fig. 5) indicate that under these conditions the trialkylammonium group remained untouched. Proceeding from this, the hydrolysis product of the diquaternary salt (V) should be assigned structure (VIII).

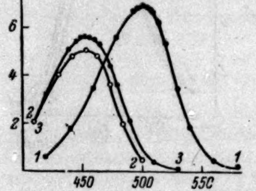


Figure 5. Absorption curves of the merocyanines. 1) [VII, A = $N(C_2H_5)_2$], 2) [VII, A = $N(C_2H_5)_2$] + + 250 moles HCl, 3) (VIII).

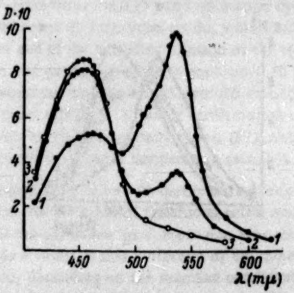


Figure 6. Absorption curves of the quaternary salt (V, X = ClO_4 after heating in 50% alcohol for various periods of time.
1) 5 min., 2) 15 min., 3) 30 min.

In the hydrolysis of quaternary salts (II) and (V) it was observed that this reaction, depending on the nature of the heterocylic parts in these dyes and the solution concentrations, proceeds at a variable rate. To elucidate the character of this relationship we ran some comparative experiments on the hydrolysis of the indicated compounds and the earlier described [2] benzothiazole derivative (II, A = H). For this purpose $1.6 \cdot 10^{-2}$ M solutions of the quaternary salts in 50% ethyl alcohol were heated on the boiling water bath, and after definite time intervals the absorption spectra of samples of the reaction solution (0.5 ml), diluted to 20 ml with anhydrous ethyl alcohol, were measured on an SF-2 spectrophotometer. The experimental results are shown in Figs. 6-8. For the quaternary salt with the 6-nitrobenzothiazole portion (II, $A=NO_2$) it proved impossible to follow the hydrolysis process with time due to the extremely small solubility of the hydrolysis product. In this case the total duration of the reaction (20 minutes) was established by the disappearance of the starting quaternary salt in the reaction mixture.

From the data obtained by us it follows that the fastest hydrolysis rate is shown by the quaternary salts containing heterocyclic parts, the basicity of which is reduced by the introduction of electronegative substituents [NO_2 and $^+NCH_3(C_2H_5)_2$]. The decomposition of these salts is nearly complete in 20-30 minutes, while in the case of the benzothiazole derivative this requires 1 hour, and in the case of the 6-diethylaminobenzothiazole derivative – 2.5 hours (Figs. 7-8). In accord with this, a hydrochloric acid-containing alcohol solution of the quaternary salt (II, $A=N(C_2H_5)_2$) shows considerably faster hydrolysis than does the neutral solution, which is associated with the transition of this compound when acidified with hydrochloric acid to the less stable diquaternary salt (VI).

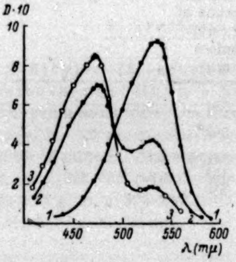


Figure 7. Absorption curves of the quaternary salt (II, A = H, $X = ClO_4$ after heating in 50% alcohol for various periods of time.

1 – 0 min., 2 – 30 min., 3 – 60 min.

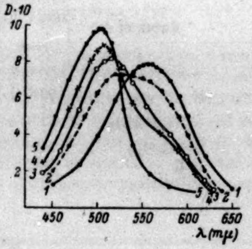


Figure 8. Absorption curves of the quaternary salt (II, $A=N(C_2H_5)_2$, $X=ClO_4$ after heating in 50% alcohol for various periods of time.

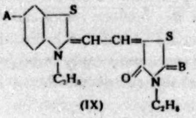
1 – 0 min., 2 – 30 min., 3 – 60 min., 4 – 90 min., 5 – 150 min.

A retardation of the hydrolysis with increase in the basicity of the heterocyclic parts in the quaternary salts of the merocyanines studied by us can be explained if it is considered that here the operating reagent is the nucleophilic hydroxyl ion. Consequently, the rate of this process will be determined by the magnitude of the positive charge, originating on the carbon atom in the 2 position of the rhodanine ring as the result of the removal of electrons from it by the nitrogen atom, bearing a positive charge.

As in the merocyanine series of rhodanine derivatives, the electron shift in the polymethine chromophore increases with increase in the basicity of the heterocyclic part in the quaternary salts. As a result of this the cationic charge of the nitrogen atom is partially saturated, which should attract a reduction of the positive charge on the 2 carbon atom and in that way a retardation of the hydrolysis reaction. From this it follows that a reduction in the basicity of the heterocyclic part should, in reverse, facilitate the hydrolysis process, which finds itself in complete accord with our obtained data.

The absorption maxima of all of the synthesized dyes are presented in Tables 1-2. As had already been mentioned earlier [1, 12], the merocyanines with the 3-ethylthiazolidin-2,4-dione portion (IX, B = O) (Table 1) are much more highly colored than the corresponding 3-ethylthiazolidin-2-thion-4-one derivatives (B = S) (Table 1). In both groups of merocyanines a replacement of the hydrogen atom in the 6 position of the benzothiazole part by the diethylamino group causes a bathochromic shift of the absorption maximum (by 30-33 mμ. Salt-formation at the diethylamino group as the result of the addition of hydrochloric acid [$NH(C_2H_5)_2$] or dimethyl sulfate [$\overset{+}{N}CH_3(C_2H_5)_2$] leads to a sharp increase in the color. It is interesting to mention that the absorption maxima of these dyes are substantially shifted toward shorter wavelengths (by 12-17 mμ) when compared with the corresponding unsubstituted compounds, whereas in the series of quaternary salts (Table 2) and thiacarbocyanine dyes [7] the difference in absorption in this case is slight (2-4 mμ).

TABLE 1



(IX)

Value of A	Absorption maxima of the merocyanines (in mμ)		Hypsochromic shift in the transition	Absorption maxima of the carbocyanines (in mμ)
	B=S	B=O	B=S→B=O	
H	524[11]	472[2]	52	558
$\overset{+}{N}CH_3(C_2H_5)_2$	510	456	54	562*
$\overset{+}{N}H(C_2H_5)_2$	512	455	57	561[7]
NO_2	528	478	50	583
$N(C_2H_5)_2$	557	502	55	618

This is apparently explained by the quite high degree of asymmetry shown by the merocyanines of this series of benzothiazole derivatives (a hypsochromic shift of 24.5 mμ for the dye (IX, A=H, B=S) [13]), and consequently a greater sensitivity to various structural changes [14] when compared with the corresponding quaternary salt (Table 2, A=H (a hypsochromic shift of 6 mμ **).

In the transition from the merocyanine derivatives of 3-ethylrhodanine to the quaternary salts of structure (II) and (V) the absorption maximum is shifted toward longer wavelengths, in which connection the value of this shift decreases with increase in the basicity of the heterocyclic parts and becomes equal to zero for the 6-diethylamino-substituted derivatives (Table 2).

It could be expected that a further increase in the basicity of the heterocyclic parts in the quaternary salts of structure (I) will lead to a hypsochromic shift of the absorption maximum of these compounds when compared with the starting merocyanine derivatives of 3-ethylrhodanine.

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* I. I. Levkoev was kind enough to furnish us with the absorption maximum of this dye.

** The hypsochromic shift for this salt was calculated in the usual manner, proceeding from the values of the absorption maxima of the corresponding symmetrical thiacarbocyanine (558 mμ) and the quaternary salt of the oxanine with the 2-methylmercaptothiazolin-4-one portions (526 mμ).

In conclusion we would like to mention that only the use of the chromatographic method in combination with the spectrometric measurements made it possible to show up a series of secondary processes and establish the structure of the resulting products.

TABLE 2

Value of A	Absorption maxima (in mμ)		Shift of absorption maximum (in mμ)
	merocyanines (IX, B=S)	quaternary salts (II)	
$\overset{+}{N}CH_3(C_2H_5)_2$	510	539	29
$\overset{+}{N}H(C_2H_5)_2$	512	538	26
NO_2	528	549	21
H	524[11]	536	12
$N(C_2H_5)_2$	557	557	0

EXPERIMENTAL•

I. Synthesis of Dimethinemerocyanine Dyes (III)

3-Ethyl-5-(3'-ethyl-6'-nitrobenzothiazolin-2'-ylideneethylidene)thiazolidin-2-thion-4-one (III, A = NO_2). A mixture of 0.76 g of 2-methyl-6-nitrobenzothiazole and 0.8 g of ethyl p-toluenesulfonate was heated for 22 hours in an oil bath at 120-125° To the obtained quaternary salt was added 1.2 g of 3-ethyl-5-acetanilinomethylenerhodanine and 20 ml of pyridine, and the mixture was boiled for 30 minutes. The next day the separated dye was filtered and washed with alcohol. Yield 0.52 g (33%), m. p. 328-330° (with decomp.). The product was purified by boiling twice with ethyl alcohol. Weight 0.44 g, m. p. 329-330° (with decomp.). Lustrous red-violet prisms. Its absorption maximum in ethyl alcohol lies at 528 mμ.

Found %: N 10.87. $C_{16}H_{15}O_3N_3S_3$. Calculated %: N 10.68.

3-Ethyl-5-(3'-ethyl-6'-diethylaminobenzothiazolin-2'-ylideneethylidene) thiazolidin-2-thion-4-one (III, A = $N(C_2H_5)_2$). A mixture of 4.8 g of 6-diethylamino-2-(β-anilinovinyl)benzothiazole ethiodide, 1.61 g of 3-ethylrhodanine, 5 ml of pyridine, 5 ml of acetic anhydride and 1.01 g (1.4 ml) of triethylamine was heated for 1 hour on the water bath at 80-85° (in the bath). The separated dye was filtered and washed with ethyl alcohol. Yield 2.9 g (70%), m. p. 198° (with decomp.). For purification the product was dissolved in 200 ml chloroform, and the solution was filtered through a layer of aluminum oxide, on which the blue dye impurity was tenaciously adsorbed. The chloroform was vacuum-distilled, and the residue was recrystallized from ethyl alcohol (1 g from 275 ml). Weight 2.5 g, m. p. 200° (with decomp.). Lustrous green needles, soluble in alcohol, benzene and ether. Its absorption maximum in ethyl alcohol lies at 557 mμ; and in acid-containing alcohol solution (250 moles of HCl per mole of dye) at 512 mμ (Fig. 2).

Found %: N 9.80. $C_{20}H_{25}N_3S_3$. Calculated %: N 10.01.

The blue dye was desorbed from the aluminum oxide with chloroform, containing 5-10% ethyl alcohol. From the shape of the absorption curve and the position of the maximum in ethyl alcohol (618 mμ) this compound is identical with 3,3'-diethyl-6,6'-bisdiethylaminothiacarbocyanine iodide.

•With the assistance of M.V. Krylova.

II. Synthesis of Quaternary Salts of Dimethinemerocyanines

2-Methylmercapto-5-(3'-ethyl-6'-nitrobenzothiazolin-2'-ylideneethylidene) thiazolin-4-one Ethyl Methyl Sulfate (II, A $=NO_2$, X $=CH_3SO_4$). A mixture of 0.39 g of 3-ethyl-5-(3'-ethyl-6'-nitrobenzothiazolin-2'-ylideneethylidene) thiazolidin-2-thion-4-one (III, A$=NO_2$) and 0.38 g of dimethyl sulfate was heated for 1 hour in an oil bath at 140-145° (in the mixture). The quaternary salt after cooling was washed with absolute ether [*] with rubbing and purified by precipitation from an alcohol solution (60 ml) with ether (200 ml). Yield 0.26 g (50%), m. p. 203-204° (with decomp.). Dark-red needles, soluble in water and alcohol, and insoluble in benzene and ether. Its absorption maximum in ethyl alcohol lies at 549 mμ.

Found %: N 8.01. $C_{18}H_{21}O_7N_3S_4$. Calculated %: N 8.09.

Ethyl Perchlorate (II, A$=NO_2$, X$=ClO_4$). The quaternary salt, obtained the same as the preceding from 0.39 g of the merocyanine (III, A$=NO_2$) and washed with ether, was dissolved in 10 ml of methyl alcohol, and the solution was poured into 8 ml of a 10% alcoholic solution of sodium perchlorate. The resulting precipitate was filtered and washed with ethyl alcohol and ether. Yield 0.28 g (55%), m. p. 246° (with decomp.). Dark-red needles, much more difficultly soluble in alcohol than the corresponding methyl sulfate. Its absorption maximum in ethyl alcohol lies at 549 mμ.

Found %: N 8.15. $C_{17}H_{18}O_7N_3S_3Cl$. Calculated %: N 8.27.

2-Methylmercapto-5-(3'-ethyl-6'-diethylaminobenzothiazolin-2'-ylideneethylidene)thiazolin-4-one Ethyl Perchlorate (II, A$=N(C_2H_5)_2$, X$=ClO_4$]. 0.42 g of 3-ethyl-5-(3'ethyl-6'-diethylaminobenzothiazolin-2'-ylideneethylidene)thiazolidin-2-thion-4-one (III, A$=N(C_2H_5)_2$) was dissolved with heating in 10 ml of toluene, then 0.38 g of dimethyl sulfate was added, and the solution was boiled for 40 minutes in an oil bath. The hot toluene was decanted from the tarry precipitate found on the bottom of the flask. The latter was washed with ether, dissolved with slight warming in 7 ml of ethyl alcohol, and the solution was poured into 4 ml of a 20% alcoholic solution of sodium perchlorate. After 3 hours the precipitate was filtered and washed with alcohol and ether. Weight 0.47 g, m. p. 227° (with decomp.). For purification the product was dissolved in 200 ml of chloroform, containing 3% ethyl alcohol, and the solution was filtered through a layer of aluminum oxide, on which the impurities were tenaciously adsorbed, forming two narrow colored zones: the upper one colored purple and the other directly adjacent to it with an orange color. Washing the adsorption column with a mixture of chloroform and ethyl alcohol (9:1) removed traces of the principal dye, and the orange layer showed a more distinct separation from the purple layer. The solvent was vacuum-distilled, and the residue was washed with ethyl alcohol (50 ml) at the boil. Weight of the washed dye 0.26 g, m. p. 235° (with decomp.). The addition of 200 ml of ether to the alcohol filtrate gave an additional 0.1 g of the dye with the same melting point. Total yield 0.36 g (67.4%). Fine dark-green needles, readily soluble in water, more difficultly soluble in alcohol and chloroform, and insoluble in benzene and ether. Its absorption maximum in ethyl alcohol lies at 557 mμ; and in acid-containing alcohol solution (250 moles of HCl per mole of dye) at 538 mμ (Fig. 1).

Found %: N 7.80. $C_{21}H_{28}O_5N_3S_3Cl$. Calculated %: N 7.86.

The adsorption column was dried slightly, and the colored layers of aluminum oxide were mechanically separated and separately extracted with ethyl alcohol. The purple dye showed an absorption maximum at 539 mμ and the orange dye at 510 mμ. The alcohol extract of the orange dye was evaporated in vacuo to dryness, and the residue was washed by boiling with 3 ml of chloroform. Weight 0.01 g, m. p. 224-225°.

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[*] Dry solvents were used in the synthesis of the quaternary salts described in this section.

From the shape of the curve and the position of the absorption maximum it is identical with dye (IV) (see below).

2-Methylmercapto-5-(3'-ethyl-6'-methyldiethylammoniumbenzothiazolin-2'-ylideneethylidene)thiazolin-4-one Ethyl Diperchlorate (V, X=ClO_4). A mixture of 0.42 g of 3-ethyl-5-(3'-ethyl-6'-diethylaminobenzothiazolin-2'-ylideneethylidene) thiazolidin-2-thion-4-one (III, A=$N(C_2H_5)_2$) and 0.38g of dimethyl sulfate was heated for 15 minutes at 130° (in the mixture). The obtained product was washed with ether, dissolved with short heating in 10 ml of methyl alcohol, and the solution poured into 10 ml of a 20% methanol solution of sodium perchlorate. After 3 hours the precipitate was filtered and washed with alcohol and ether. Weight 0.53 g, m. p. 235° (with decomp.). The product was purified from the impurity of more soluble quaternary salt (II, A=$N(C_2H_5)_2$, X=ClO_4) by boiling with ethyl alcohol (twice with 40 ml portions), and then with chloroform until all of the indicated impurity had been removed. Weight of residue 0.24 g, m. p. 247° (with decomp.). From the alcohol filtrates by precipitation with ether (100 ml portions) we isolated two precipitates. After supplementary purification by chromatographing on aluminum oxide, the product obtained from the first fraction (0.09 g, m. p. 220°) proved to be identical with the above described 2-methylmercapto-5-(3'-ethyl-6'-diethylaminobenzothiazolin-2'-ylideneethylidene)thiazolin-4-one ethyl perchlorate (m.p. 235°, absorption maximum at 557 mμ). The precipitate, isolated from the second alcohol fraction (0.08 g, m. p. 242°) and being mainly the diquaternary salt (V), after boiling twice with chloroform had m. p. 247°. The residue weighed 0.05 g. Total yield 0.29 g (45%). Fine purple needles, soluble in alcohol insoluble in chloroform, benzene and ether. Its absorption maximum in ethyl alcohol lies at 539 mμ.

Found %: C 40.18; H 5.20; N 6.64, 6.46; S 14.67, 14.48. $C_{22}H_{31}O_9N_3S_3Cl_2$. Calculated %: C 40.73; H 4.82; N 6.48; S 14.82.

3-Ethyl-5-(3'-ethyl-6'-methyldiethylammoniumbenzothiazolin-2'-ylideneethylidene)thiazolidin-2-thion-4-one Perchlorate (IV, X=ClO_4). To a suspension of 0.32 g of 2-methylmercapto-5-(3'-ethyl-6'-methyldiethylammoniumbenzothiazolin-2'-ylideneethylidene) thiazolin-4-one ethyl diperchlorate (V, X=ClO_4) in 20 ml of hot ethyl alcohol was added 1 ml of a 21.5% water solution of sodium hydrosulfide, and the mixture was manually shaken for 30 minutes, after which it was let stand until the next day. The obtained precipitate was filtered and washed with water and alcohol. Yield 0.24 g (90%, m. p. 218° (with decomp.). For purification from a small amount of more deeply colored dye (absorption maximum in ethyl alcohol at 555 mμ) the product was boiled with benzene (3 times with 30 ml portions), after which it was recrystallized from ethyl alcohol (1 g from 500 ml). Weight 0.16 g (60%), m. p. 227 (with decomp.). Dark-red prisms, soluble in alcohol and practically insoluble in chloroform, benzene and ether. Its absorption maximum in ethyl alcohol lies at 510 m μ.

Found %: N 7.89. $C_{21}H_{28}O_5N_3S_3Cl$. Calculated %: N 7.86.

Reaction of Pyridine with 3-Ethyl-5-(3'-ethyl-6'-methyldiethylammoniumbenzothiazolin-2'-ylideneethylidene)thiazolidin-2-thion-4-one Perchlorate (IV, X=ClO_4). A solution of 0.026 g of 3-ethyl-5-(3'-ethyl-6'-methyldiethylammoniumbenzothiazolin-2'-ylideneethylidene)thiazolidin-2-thion-4-one perchlorate in 50 ml of dry pyridine was heated for 2 hours in an oil bath at 125°. Every half hour a sample (0.5 ml) was removed from the reaction mixture, the pyridine vacuum-distilled, the residue dissolved in 10 ml of ethyl alcohol, and the solution measured using an SF-2 spectrophotometer (Fig. 3). To isolate the reaction product the pyridine was vacuum-distilled, and the residue was recrystallized from 4 ml of ethyl alcohol. Weight 0.016 g (75%), m. p. 200°. Its absorption maximum in ethyl alcohol lies at 555 mμ.

III. Hydrolysis of Quaternary Salts (II) and (V) in Aqueous Alcohol Medium

3-Ethyl-5-(3'-ethyl-6'-nitrobenzothiazolin-2'-ylideneethylidene)thiazolidin-2,4-dione (VII, A=NO_2). Hydrolysis of the Quaternary Salt (II, A=NO_2, X=ClO_4). A mixture of 0.3 g of 2-methylmercapto-5-(3'ethyl-6'-nitrobenzothiazolin-2'-ylideneethylidene)thiazolin-4-one ethyl perchlorate in 100 ml of 50% ethyl alcohol was heated for 30 minutes on the boiling water bath.

Soon after the start of boiling, even before the original product had completely dissolved, a fine dark-brown precipitate began to deposit, and the copious evolution of methyl mercaptan was observed. After boiling for 20 minutes the original intense purple color changed to an orange, and the chromatographing of a sample of the reaction mixture on aluminum oxide revealed the presence of only traces of the original quaternary salt. The precipitate was filtered and washed with alcohol. Yield 0.19 g (84%), m. p. 322° (with decomp.). The dye was purified by boiling with ethyl alcohol (twice with 50 ml portions). The residue weighed 0.17 g, m. p. 325° (with decomp.). The melting point of the dye did not change after recrystallization from chloroform (1 g from 3000 ml). Fine brown prisms, very difficultly soluble in alcohol, benzene and ether, and somewhat more soluble in chloroform. Its absorption maximum in ethyl alcohol lies at 478 mμ.

Found %: N 10.95. $C_{16}H_{15}O_4N_3S_2$. Calculated %: N 11.13.

3-Ethyl-5-(3'-ethyl-6'-methyldiethylammoniumbenzothiazolin-2'-ylidene-ethylidene)thiazolidin-2,4-dione Perchlorate (VIII). (Hydrolysis of the Diquaternary Salt (V, $X = ClO_4$). A solution of 0.65 g of 2-methylmercapto-5-(3'-ethyl-6'-methyldiethylammoniumbenzothiazolin-2'-ylideneethylidene)thiazolin-4-one ethyl diperchlorate in 45 ml of 50% ethyl alcohol was heated for 45 minutes on the boiling water bath. During the heating process the original intense purple color of the solution changed to a dark-orange. The precipitate, separating after cooling, was filtered and washed with alcohol. Yield 0.37 g (71.5%), m. p. 225° (with decomp.). The dye was purified by recrystallizing twice from 25% ethyl alcohol (1 g from 150 ml). Weight 0.3 g, m. p. 243° (with decomp.). Light-brown needles, readily soluble in alcohol, more difficultly in water, and insoluble in chloroform, benzene and ether. Its absorption maximum in ethyl alcohol lies at 456 mμ.

Found %: N 7.92, 8.02. $C_{21}H_{28}O_6N_3S_2Cl$. Calculated %: N 8.11.

3-Ethyl-5-(3'-ethyl-6'-diethylaminobenzothiazolin-2'-ylideneethylidene)thiazolidin-2,4-dione (VII, $A = N(C_2H_5)_2$). (Hydrolysis of the Quaternary Salt (II, $A = N(C_2H_5)_2$, $X = ClO_4$). A solution of 0.53 g of 2-methylmercapto-5-(3'-ethyl-6'-diethylaminobenzothiazolin-2'-ylideneethylidene)thiazolin-4-one ethyl perchlorate in 160 ml of 50% ethyl alcohol was heated for 2.5 hours on the boiling water bath. During the heating process the original reddish-violet color of the solution gradually changed to a red. To isolate the reaction product the solvent was vacuum-distilled, the residue dissolved in chloroform, and the solution filtered through a layer of aluminum oxide, on which the original unreacted quaternary salt was adsorbed. The filtrate was vacuum-evaporated, and the residue (0.27 g) was recrystallized from 50% ethyl alcohol. Yield 0.2 g (50%), m. p. 159° (with decomp.). Red needles, readily soluble in alcohol, benzene and ether. Its absorption maximum in ethyl alcohol lies at 502 mμ; and in acid-containing alcohol solution (250 moles of HCl per mole of dye) at 455 mμ (Fig. 5).

Found %: N 10.37, 10.47; S 15.73. $C_{20}H_{25}O_2N_3S_2$. Calculated %: N 10.41 S 15.64.

We wish to thank I. I. Levkoev for his continued valuable advice.

SUMMARY

1. A number of new quaternary salts of the dimethinemerocyanine derivatives of 2-methylmercaptothiazolin-4-one with the 6-nitro, 6-diethylamino- or 6-methyldiethylammoniumbenzothiazole portions were synthesized.

In the reaction of dimethyl sulfate with 3-ethyl-5-(3'-ethyl-6'-diethylaminobenzothiazolin-2'-ylideneethylidene)thiazolidin-2-thion-4-one it was shown that methylation can take place at both the thiono sulfur and the diethylamino group.

2. The reactions of the synthesized quaternary salts were studied. It was established that the rate of their hydrolysis in aqueous alcohol medium decreases with increase in the basicity of the heterocyclic part in the compounds.

The reaction of 2-methylmercapto-5-(3'-ethyl-6'-methyldiethylammoniumbenzothiazolin-2'-ylideneethylidene)thiazolin-4-one ethyl diperchlorate with sodium hydrosulfide gave the previously unknown dimethinemerocyanine with a 6-methyldiethylammoniumbenzothiazole portion.

3. The optical properties of the synthesized dyes were studied. It was shown that introduction of a methyldiethylammonium group in the 6 position of the thiadimethinemerocyanine derivatives of 3-ethylrhodanine and 3-ethylthiazolidin-2,4-dione causes a substantial shift of the absorption maximum toward shorter wavelengths when compared with the corresponding unsubstituted dyes.

A bathochromic shift of the absorption maximum is observed in the transition of the merocyanine derivatives of 3-ethylrhodanine to the quaternary salts, the magnitude of which decreases with increase in the basicity of the heterocyclic parts in the investigated dyes.

LITERATURE CITED

[1] Z. P. Sytnik, I. I. Levkoev and M. V. Deichmeister, J. Gen. Chem., 21, 768 (1951). (T. p. 847).*

[2] Z. P. Sytnik, I. I. Levkoev, M. V. Deichmeister and L. D. Zhilina, J. Gen. Chem., 22, 1228 (1952). (T. p. 1273).*

[3] Brit. Patent 505,839.

[4] A. I. Kiprianov and E. D. Sych, Trans. Inst. Chemistry, Kharkov State Univ., 2, 16 (1936); b) Memoirs Inst. Chemistry Acad. Sci. USSR, 8, 103 (1946).

[5] H. Barbier, Bull. Soc. Chim., (4) 27, 427 (1920).

[6] G. T. Pilyugin and Z. Ya. Krainer, J. Gen. Chem., 23, 634 (1953) (T. p. 661).*

[7] A. I. Kiprianov and I. K. Ushenko, J. Gen. Chem., 15, 207 (1945).

[8] I. I. Levkoev, N. N. Sveshnikov, I. N. Gorbacheva and A. F. Vompe, Trans. Sci.-Res. Inst. Motion Pictures and Photography, No. 7, 30 (1944).

[9] Fr. Patent 942,826.

[10] J. D. Kendall, J.D. Fry, J. Chem. Soc., 1951, 1716.

[11] M. V. Deichmeister, Z. P. Sytnik, I. I. Levkoev and E. B. Lifshits, J. Gen. Chem., 24, 898 (1954). (T. p. 897).*

[12] Z. P. Sytnik, M. V. Deichmeister, T. G. Gnevysheva and L. D. Zhilina, Author's Certificate, USSR No. 81,881.

[13] M. V. Deichmeister, Z. P. Sytnik and E. B. Lifshits, J. Gen. Chem., 22, 166 (1952). (T. p. 209).*

[14] L. G. S. Brooker, Rev. of mod. Phys., 14, 275 (1942).

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* T. p. = C. B. Translation pagination.

THE ADDITIVE CAPACITY OF A DOUBLE BOND AT A TERTIARY CARBON

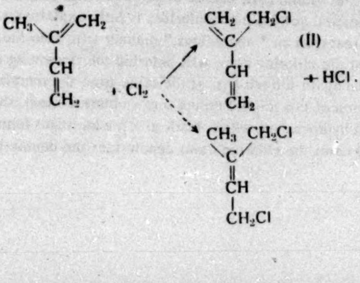
REACTION OF CHLORINE WITH 1,3-DIENES

D. Tishchenko, A. Abramova and E. Yarzhemskaya

The addition reactions of the 1,3-dienes have been studied in some detail. All of the investigators have attempted to establish whether the given addition reaction is in the 1,4 position (Thiele's rule), the 1,2 position, or the 3,4 position (exception to the Thiele rule). It is exactly from this viewpoint that these transformations of the 1,3-dienes have been examined in the latest edition of W Hückel's book [1]. The possibility of some other mechanism for the reaction, for example, of halogens with 1,3-dienes is not even considered, despite a number of experimentally established facts. The evolution of hydrogen halide has repeatedly been observed in this reaction. In some cases the investigators limit themselves to a quantitative determination of the hydrogen halide and to establishing the relationship between its amount and the structure of the 1,3-diene being halogenated [2], in other cases this "irregular" phenomenon is simply ignored and the isolated, but not postulated, reaction products [3] are not studied, while in still other cases, having isolated a halide with the same degree of unsaturation as the starting 1,3-diene, an attempt is made to justify the classic addition scheme by postulating the decomposition of the initially formed dihalide with the liberation of hydrogen halide [4].

The liberation of hydrogen halide in the halogenation of 1,3-dienes was observed only when disturbances, either central or terminal, were present in a conjugated system of double bonds, i.e., when even a single tertiary carbon atom was present at a double bond. Consequently, it could be thought that this reaction is a particular case of the M D. Lvov reaction, studied in detail by one us in the series of ethylene derivatives and terpenes [5]. In this reaction an ethylene derivative gives with chlorine mainly a monochloride of the allyl type with a shifted double bond ("anomalous" reaction) and a lesser amount of the saturated dichloride ("classical" reaction). The mechanism proposed by us for the Lvov reaction is generally accepted [6].

By chlorinating isoprene, Jones and Williams [4] obtained the monochloride C_5H_7Cl with b. p. 107°, established the presence of a system of conjugated double bonds in it by its condensation with α-naphthoquinone and by preparing the sulfone, and postulated, but did not prove, that structurally it was 1-chloro-2-methyl-1,3-butadiene (I). One of us had obtained this chloroisoprene earlier and had proved its structure [7]. Its boiling point is 7° lower (100°) than the chloroisoprene obtained by the English authors, and in our opinion, the latter is 2-chloromethyl-1,3-butadiene (II), formed from isoprene by the Lvov reaction:



The experimental verification of our postulation revealed its validity: the isoprene monochloride contains saponifiable chlorine and when oxidized with potassium permanganate it gives chloroacetic acid, which is possible only for structure (II). Chloride (II) can be assumed to be the product obtained by the replacement of a hydrogen in the methyl group of isoprene by chlorine (" substitution scheme " of the American chemists), similar to the formation of isobutenyl chloride from isobutylene, although this scheme has already been refuted for isobutylene [6]. To check the applicability of the Lvov reaction to other 1,3-dienes with a tertiary carbon atom we studied the reaction of chlorine, under the conditions described by us earlier [5], with still three other hydrocarbons: 2,3-dimethyl-1,3-butadiene, 2,4-dimethyl-1,3-pentadiene and 2,5-dimethyl-2,4-hexadiene. The specific proportion of the Lvov reaction (monochloride + HCl), based on the evolved hydrogen chloride, ranged from 55 to 73%. Consequently, the Lvov reaction was the main reaction, and addition in the 1,4, 1,2 and 3,4 positions was subordinate. In this way we established for the 1,3-dienes a new exception to the Thiele rule and showed that double bonds can react separately when either the central or terminal alkyls are disturbed.

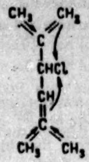
A study of the structure of the obtained chlorodienes, being chlorides of the allyl type (it was shown in all cases that their chlorine atom is easily hydrolyzed), presented certain difficulties due to allylic rearrangements. In two cases the monochloride was a mixture of allylic isomers, which was established by ozonolysis.

The chlorination of 2,3-dimethyl-1,3-butadiene gave 2-chloromethyl-3-methyl-1,3-butadiene and 2,3-dimethyl-1,4-dichloro-2-butene. Ozonolysis and subsequent oxidation of the monochloride gave acetic and chloroacetic acids, and ozonolysis of the dichloride gave chloroacetone, which was sufficient to confirm the indicated structure. Allylic rearrangement of the monochloride fails to change its structure, the same as is true for the monochloride of isoprene (II).

In accord with the earlier developed theories [5], in the chlorination of 2,4-dimethyl-1,3-pentadiene the 3,4 bond, as being the most highly branched, should show preferential reaction, with the formation of 2,4-dimethyl-3-chloro-1,4-pentadiene (III). The latter can isomerize to 2-methyl-4-chloromethyl-1,3-pentadiene (IV). The ozonization of (III) gives formaldehyde, formic acid and 3-chloro-2,4-pentanedione, while the ozonization of (IV) gives formaldehyde, formic acid, chloroacetone and methylgyloxal. Actually, in the water-insoluble ozonolysis products we found chloroacetone and a substance, in its elementary composition closely resembling a chloropentadione, and giving acetic acid when oxidized. In the water-soluble products we found formaldehyde, formic acid and chloride ion. We were unable to isolate methylglyoxal and pyrotartaric acid, but indirectly their presence was shown with great probability: after exhaustive extraction with ether and decomposition with water, only formic acid was found in the alkaline aqueous layer of the ozonolysis products prior to oxidation, while after oxidation with potassium permanganate at 100° to a permanent pink color only acetic acid was found. The latter could have also been formed as the result of oxidizing any chloropentanedione not extracted by the ether. The fact that the chloropentanedione and chloroacetone were obtained in the ozonolysis proves the presence of chlorides (III) and (IV). Since the isomerization of chloride (IV) (primary, conjugated) to chloride (III) (secondary, not conjugated) is not very probable, it must be assumed that (III) is the primary chlorination product of 2,4-dimethyl-1,3-pentadiene, which proves the presence of the "anomalous" Lvov reaction in the given instance.

The chlorination of 2,5-dimethyl-2,4-hexadiene was somewhat peculiar: instead of the monochloride, the diene dichloride was obtained, proving to be a mixture of 2,5-dimethyl-3,4-dichloro-1,5-hexadiene (V, primary product), 2,5-dimethyl-3,6-dichloro-1,4-hexadiene (VI, single allylic rearrangement) and 2,5-dimethyl-1,6-dichloro-2,4-hexadiene (VII, double allylic rearrangement). The formation in this case of specifically the diene dichloride, and not the monochloride, is fully explained with our theory [5]. If one of the equivalent double bonds reacts in an " anomalous " manner with chlorine, then in the diene monochloride the negative inductive effect of the chlorine atom will polarize the remaining double bond in the " necessary " direction and will depolarize the again formed (A); at the same time the remaining double bond, being subjected to the concordant action of two methyl groups and a chlorine atom, should be more reactive than the double bonds of the original hydrocarbon, which leads to a predominant formation of the diene dichloride. In three of the above examined cases the chlorine atom depolarizes the double bonds of the monochlorides, and they are retained.

The ozonolysis of (V), (VI) and (VII) should give 3,4-dichloro-2,5-hexanedione, chlorobutanonal, glyoxal, chloroacetone, formaldehyde and formic acid.

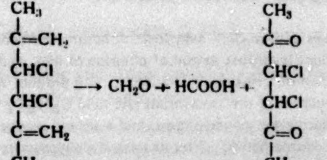

CH₃
CH₃
C
CHCl
CH
C
CH₃
CH₃

(A)

Actually, all of these products were obtained. Since a 2-fold allylic rearrangement of the conjugated diprimary dichloride (VII) into the disecondary not conjugated dichloride (V) is improbable, then it must be assumed that (V) is the primary reaction product, which again supports the validity of our mechanism for the chlorination of derivatives with a tertiary carbon atom at a double bond and refutes the " substitution " chlorination of the American school.

These data again needlessly show to what extent an attempt to explain facts with the generally accepted theories without experimental verification of the offered explanations is incompatible with a knowledge of the truth: Jones and Williams believed that isoprene can add chlorine

(V)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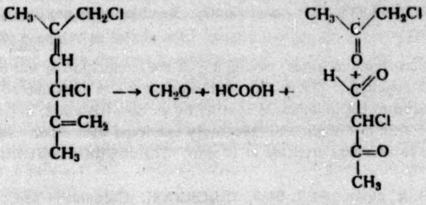
C=CH₂
CHCl
CHCl
C=CH₂
CH₃
CH₂O + HCOOH +
CH₃
C=O
CHCl
CHCl
C=O
CH₃

(VI)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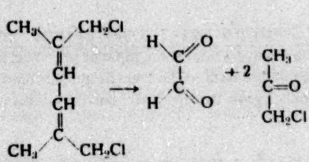
CH₂Cl
C
CH
CHCl
C=CH₂
CH₃
CH₂O + HCOOH +
CH₃
CH₂Cl
C
O
H
O
C
CHCl
C=O
CH₃

(VII)


CH₃
CH₂Cl
C
CH
CH
C
CH₃
CH₂Cl
H
C
O
C
H
O
+ 2
CH₃
C=O
CH₂Cl

only in the 1,2 or 1,4 positions, and consequently they assumed the monochloride obtained by them to be 1-chloro-2-methyl-1,3-butadiene, the product of hydrogen chloride cleavage from 1,2-dichloro-2-methyl-3-butene. In chlorinating 2,3-dimethyl-1,3-butadiene, R. Ya. Levina and co-workers [3] isolated a fraction that boiled below the dichloride, and left it unstudied, apparently assuming its formation to be somewhat accidental. As a matter of fact, as shown by us, in the case of disturbed aliphatic 1,3-dienes the Lvov reaction is the main reaction, and the reactions for addition in the 1,2, or 3,4, or 1,4 positions are subordinate.

EXPERIMENTAL

Chlorination of Isoprene (done by E. Ya. Yarzhemskaya). The isoprene was obtained by the dehydration of dimethylvinylcarbinol over magnesium sulfate at 230-260°. B. p. 33.8–34.8°, d_4^{20} 0.679. The chlorination conditions have been described earlier [5]. After distilling off the isoprene the chlorides were distilled through a column with an efficiency of about 10 theoretical plates, and the fraction with b. p. 38-40° at 70 mm was isolated.

d_4^{20} 0.955, n_C^{15} 1.4651.

Found %: Cl 34.7, 34.6. C_5H_7Cl. Calculated %: Cl 34.6.

The monochloride condenses with maleic anhydride in boiling benzene with the evolution of hydrogen chloride. The condensation product is almost devoid of chlorine (0.6%), and melts in an open capillary with darkening and the sublimation of white crystals at 270-280°. The product was found to have an acid equivalent of 61.9; for the dianhydride of the tetracarboxylic acid $C_{13}H_{12}O_4$ the calculated equivalent is 58. Hydrogen chloride was split off during the condensation, and a second molecule of maleic anhydride added to the new system of conjugated double bonds. After heating a weighed sample of the monochloride with a solution of potassium acetate in acetic acid for 30 hours on the water bath we obtained 42% of the calculated amount of potassium chloride, and after boiling the monochloride with alcoholic potassium hydroxide solution for 10 hours we obtained 83% KCl; consequently, the chlorine is not located at a double bond (structure II).

Oxidation. With stirring and water cooling 3 g of the monochloride was oxidized with a solution of 26.5 g of potassium permanganate. The excess oxidizing agent was decomposed with hydrogen peroxide. The filtrate was separated from the manganese dioxide by suction-filtration, evaporated to 40 ml, acidified with hydrochloric acid to Congo, and repeatedly extracted with ether. The ether was removed from the extracts, and the residue was distilled at 10 mm. The distillate crystallized (2.1 g).

Found %: Cl 37.3, 37.3; equiv. 94.7, 94.5. $CH_2ClCOOH$. Calculated %: Cl 37.5; equiv. 94.5.

The chloride of composition $C_6H_8Cl_2$ was not investigated, since its structure had been reliably established earlier [4].

Chlorination of 2,3-Dimethyl-1,3-butadiene (done by A. F. Abramova). The hydrocarbon was obtained by the dehydration of the pinacol [8]. The fraction with b. p. 70-71° was taken; its constants agreed with the literature data. The specific proportion of the "anomalous" reaction was 60%. Distillation of the reaction product gave two fractions, boiling within narrow limits: a) 54-55° at 40 mm, and b) 85-86° at 20 mm.

Fraction "a": d_4^{26} 0.956, n_D^{26} 1.4729, MR_D 34.16; Calc. 33.84.

Found %: Cl 29.9, 29.9. C_5H_9Cl. Calculated %: Cl 30.5.

The heating of a weighed sample of the monochloride for 16 hours on the water bath with a solution of potassium acetate in acetic acid gave 67% of the calculated amount of potassium chloride. Consequently, the chlorine is not found at a double bond, i.e., the monochloride should be 2-chloromethyl-3-methy-1,3-butadiene, which was confirmed by ozonization and subsequent oxidation of the ozonolysis products to the acids with potassium permanganate. Here we obtained carbonic acid, acetic acid (% Ag in the salt 64.4, 64.6) and chloroacetic acid (crystals with m. p. 58-61°; equiv. 96.7; % Cl 37.3).

Fraction " b " crystallized, and after pressing on paper the crystals had m. p. 36-37° [3]. Their ozonolysis gave only chloroacetone; consequently, they are 2,3-dimethyl-1,4-dichloro-2-butene.

Chlorination of 2,4-Dimethyl-1,3-pentadiene. The directions of R. Ya. Levina and co-workers[9] were used to obtain the hydrocarbon, b. p. 94.5-96°, d_4^{20} 0.740, n_D^{20} 1.4454. The specific proportion of the " anomalous " reaction was 73%. Distillation of the reaction product gave, besides starting hydrocarbon, only one constant boiling fraction with b. p. 27° at 4 mm., in composition corresponding to the monochloride (a). It was obtained in a yield of 48 g from 101 g of reacted hydrocarbon. The higher boiling fraction distilled at around 45° at 0.5 mm; from its chlorine content (32-33%) it corresponded to a mixture of the monochloride and dichloride (monochloride 27%, dichloride 45%). A second distillation through a column with an efficiency of 8-10 theoretical plates at a 15-20 reflux ratio failed to effect separation. Apparently, the monochloride and dichloride, in the given weight ratio, give a constant boiling mixture. From the high-boiling residue we isolated 12 g of substance, in its composition approximating the trichloride: %Cl 50.8, for $C_7H_{11}Cl_3$, 52.3.

Fraction " a ". B. p. 27° and 4 mm, d_4^{20} 0.940, n_D^{20} 1.4785, MR_D 39.32; calc. 38.46.

Found %: Cl 27.4, 27.0. $C_7H_{11}Cl$. Calculated %: Cl 27. 2.

The oxidation of the monochloride with excess potassium permanganate, as was to be expected for chlorides (III) and (IV), gave only acetic acid and carbonic acid.

The ozonolysis of the monochloride was run in chloroform solution, after which the solution was stirred with cold water and a small amount of manganese dioxide (to decompose the H_2O_2) until all of the peroxide was destroyed, which required 24 hours. The chloroform layer was separated from the water layer. Formaldehyde was qualitatively shown to be present in the water layer; the total acidity of the water layer was 1.76 g-equiv., calculated on the basis of the ozonized monochloride; of this acidity 0.33 g-equiv. went to hydrochloric acid, 0.80 g-equiv. to formic acid (determined by the Scala method), and 0.63 g-equiv. to some acid other than acetic, since the steam-distillation of a portion of the water layer gave only formic acid in the distillate. p-Nitrophenylhydrazine gave a red precipitate with a portion of the water layer, but its recrystallization from various solvents failed to give any crystals with a sharp melting point; consequently, the possible presence of pyrotartaric acid had to be established indirectly: a portion of the water layer was neutralized and extracted 16 times with an equal volume of ether, after which the water layer was oxidized with excess permanganate solution at 90°. Only carbonic acid and acetic acid, isolated as the silver salts, were found in the oxidized solution.

The chloroform was removed from the chloroform layer by distillation through a column, while the residue was distilled on the water bath at 12 mm to give only one fraction (0.3 mole) with b. p. 26 – 27°, d_4^{20} 1.178.

Found %: Cl 37.1. C_3H_5OCl. Calculated %: Cl 38.4.

This fraction was a liquid with a sharp, lachrymatory odor. A semicarbazone was prepared from it, which after recrystallization from alcohol-benzene mixture had m. p. 170°.

Found %: Cl 23.7, 24.1. $C_4H_8ON_3Cl$. Calculated %: Cl 23.7.

The substance is chloroacetone. Decomposition with the evolution of gases was observed when an attempt was made to vacuum-distill a portion of the residue obtained from the distillation of the chloroacetone. The residue gave a sharp reaction for peroxide with potassium iodide. The residue was analyzed without being distilled.

Found %: C 38.4, 38.4; H 4.9; Cl 27.7, 27.9. $C_5H_7O_2Cl$. Calculated %: C 44.6; H 5.2; Cl 26.4.

The oxidation of a portion of the residue with excess permanganate gave only acetic acid, approximately 2 moles per mole of the chloropentanedione. It is extremely probable that the residue was mainly the 3-chloro-2,4-pentanedione and its peroxide.

Chlorination of 2,5-Dimethyl-2,4-hexadiene. The hydrocarbon was obtained by the Kucherov method [10], involving the reaction of magnesium with isobutenyl chloride and isomerization of the resulting 2,5-dimethyl-1,5-hexadiene. M. p. 13°, d_4^{20} 0.763, n_D^{20} 1.4752.

The chlorination was run in chloroform solution. The specific proportion of the " anomalous " reaction was 55%. We took 122 g of the hydrocarbon; after distilling off the excess hydrocarbon at 12 mm through a column of 8-10 theoretical plates the pressure was reduced to 0.5 mm; 42 g of a fraction with b. p. 40-42° was obtained:

d_4^{20} 1.042, n_D^{20} 1.4757, MR_D 48.43; calc. 47.94.

Found %: Cl 39.1, 39.6. $C_8H_{12}Cl_2$. Calculated %: Cl 39.6.

The ozonization of 14 g of the dichloride was run in chloroform solution; the solution was stirred with ice water for 24 hours. The qualitative test for formaldehyde was positive. The chloroform and water layers were separated. The chloroform was removed from the first layer by distillation through a column at 42 mm, while the residue was distilled through a Vigreaux column to give: a) b. p. 29 – 32° and 18 mm, 2.5g; b) 48 –52° and 2 mm, 4.5g; b) 96 – 99° and 1 mm, 3.2g.

Fraction " a " was a lachrymatory liquid, d_4^{20} 1.19, % Cl 42.2, b. p. at 760 mm 110 – 119°, and represented chloroacetone with chloroform as impurity. The semicarbazone was prepared, containing 24.6% Cl, while calculated Cl for $C_4H_8ON_3Cl$ is 23.7%.

Fraction " b " : d_4^{20} 1.181, n_D^{20} 1.4482.

Found %: C 37.9, 38.1; H 6.7, 6.4; Cl 36.7, 36.3. $C_6H_8O_2Cl_2$ (dichloro diketone).
Calculated %: C 39.3; H 4.4; Cl 38.8.

The last fraction was possibly a mixture of 75% of the dichloro diketone and 25% of the ketochloroaldehyde. The oxidation of 1.75 g of the fraction with cold 3% hydrogen peroxide was run in the presence of sodium bicarbonate with ice-cooling and stirring for 24 hours. The excess peroxide was decomposed with platinum black, the Pt black was filtered, and the solution was extracted with ether. The ether was removed from the extract, the residue was crystallized, and the crystals were found to contain 39.1 and 39.2 % Cl, while for $C_7H_8Cl_2O_2$ the calculated % Cl is 38.8. The solution of salts was acidified with hydrochloric acid and extracted with ether, then the ether was removed from the extract, and the residue was dried over sulfuric acid.

Found: equiv. 119; % Cl 22.7. $C_4H_5O_3Cl$ (chloroketo acid). Calculated : equiv. 136; % Cl 26.0.

Half of fraction " c " crystallized, and the crystals were separated. The crystals had % Cl 40.5 and 40.4, while for $C_6H_8O_2Cl_2$ the calculated % Cl is 38.8. Oxidation of the crystals with excess permanganate gave only acetic acid and carbonic acid.

Formic acid (0.29 equiv. per mole of the dichloride; determined by the Scala method) and glyoxal were found in the water layer of the ozonolysis products. To determine the glyoxal a portion of the water solution was oxidized with alkaline permanganate solution, after which the filtered solution was acidified with acetic acid and precipitated with calcium chloride solution. The washed precipitate of calcium oxalate was dissolved in dilute sulfuric acid and titrated with permanganate solution. The amount of glyoxal found was 0.25 g.

SUMMARY

1. The reaction of chlorine with four conjugated dienes showing central and terminal disturbances of the conjugation was studied under conditions that assured obtaining the primary reaction products.

2. It was shown that in all of the investigated cases the main reaction is the " anomalous " Lvov reaction, while addition in the 1,4, 1,2 or 3,4 positions is subordinate.

3. The mechanism of the Lvov reaction, proposed by us earlier, is also applicable here.

4. A new exception to the Thiele rule was revealed, and it was shown that in some cases the individuality of a double bond is not suppressed by conjugation.

LITERATURE CITED

[1] W. Hückel, Theoretical principles of Organic Chemistry, I, pp 461 and on (1955). Leningrad Press, Moscow.

[2] V. I. Esafov, J. Gen. Chem., 19, 1063 (1949) (T. p. 1055); 22, 604 (1952). (T. p. 665).*

[3] For example, R. Ya. Levina and co-workers, J. Gen. Chem., 23, 725 (1953). (T. p. 755).*

[4] For example, Jones and Williams, J. Chem. Soc., 1934, 829.

[5] D. Tishchenko, J. Gen. Chem., 8, 1232 (1938); 20, 563 (1950).

[6] Burgin, Ind. Eng. Ch., 33, 384 (1941); Reeve, J. Am. Chem. Soc., 73, 4499 (1951); 74, 5369 (1952).

[7] D. Tishchenko, J. Gen. Chem., 6, 1116 (1936).

[8] I. I. Ostromyslensky, J. Russ. Phys.-Chem. Soc., 47, 1969 (1915).

[9] R. Ya. Levina and co-workers, J. Gen. Chem., 18, 1775 (1948).

[10] L. M. Kucherov, J. Russ. Phys.-Chem. Soc., 45, 1634 (1913).

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Forest Technology Academy

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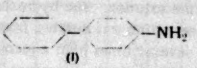
*T.p. = C.B. Translation pagination.

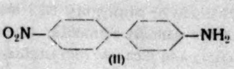
STERIC HINDRANCE AND REACTIVITY

VI. KINETICS FOR THE ACYLATION OF 2-AMINOFLUORENE AND 2-AMINO-7-NITROFLUORENE

L. M. Litvinenko and A. P. Grekov

For the purpose of establishing an interrelationship between spatial configuration and reactivity in a number of binuclear aromatic aminonitro derivatives, we have made in the course of the last two years a comparative study of the reaction kinetics for the acylation of 4-aminobiphenyl (I) and 4-amino-4'-nitrobiphenyl (II), on the one hand, and of the derivatives of these amines, containing various substituents in the 2,2'-positions (III and IV), on the other [1-4]. It was shown that an increase in the angle between the planes of the benzene rings in the transition from 4-amino-4'-nitrobiphenyl to its 2,2'-derivative, conditioned by steric hindrance between the 2,2'-substituents, leads to substantial reduction in the reactivity of the NO_2- and NH_2-groups found in the 4,4'-positions of the indicated compounds:


(I)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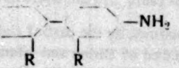
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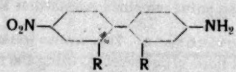
(IV)

It seemed of considerable interest to study the problem of the manner in which the reactivity of the NO_2- and NH_2-groups would be manifested through the biphenyl system if in some way the molecular geometric configuration of the biphenyl derivatives could be changed in such a manner that the angle between the planes of the benzene rings in these molecules, in contrast to the above mentioned examples, would not increase, but instead decrease. This can be achieved by closing the 2,2'-positions in biphenyl derivatives with a bridging link, as a result of which either a new 5- or 6-membered ring is formed, and the angle between the planes of the benzene nuclei in such derivatives should approach a zero value. If the bridging link for the indicated chain is the methylene group, then transition from biphenyl derivatives to a one-type fluorene derivative is realized, and in that way the desired result will be achieved, since it is known that in the fluorene molecule, in contrast to the nonplanar biphenyl molecule *, the benzene rings have a coplanar configuration, or one close to it [5-8].

In accord with the above, we studied the kinetics for the acylation of 2-aminofluorene (V) and 2-amino-7-nitrofluorene (VI) with p-nitrobenzoyl chloride in benzene solution at 25 and 50°. The data obtained here were compared with the results of our earlier studies on the acylation of some amino derivatives of biphenyl.

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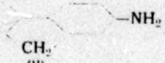
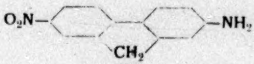
* See the literature on this problem in our previous communication of this series.


(V)


(VI)

EXPERIMENTAL

I. Preparation and Purification of Starting Substances

The benzene and p-nitrobenzoyl chloride were purified in the same manner as described earlier [1]. After preliminary purification, the amines were repeatedly recrystallized to constant melting point.

2-Aminofluorene. To a heated suspension of 7.5 g of finely divided 2-nitrofluorene [9] (recrystallized from pyridine) in 150 ml of methanol and 10 ml of 98 % hydrazine hydrate was gradually added Raney nickel, with adherence to the operational techniques described in detail in [10]. The nitro compound went into solution after about 1.5 hours, and the reaction was completed by boiling the mixture• (cessation of gas-evolution [10]).

After filtering while hot the alcohol was distilled off to a small volume, and the amine was precipitated with water. The yield was quantitative; m. p. 128-128.5°.

The amine was purified by dissolving it in benzene (treatment with activated carbon) and then precipitating it as the hydrochloride by passing dry HCl into the solution. The hydrochloride was decomposed by heating in methanol, saturated with dry ammonia. The free amine was isolated from the methanol solution by the addition of water, and then was recrystallized several times from aqueous methanol (2:1), in which connection the melting point remained constant at 128-128.5° (in the literature [9] – 127.5°).

2-Amino-7-nitrofluorene. This amine was obtained by the partial reduction of 2,7-dinitrofluorene [12] (recrystallized from nitrobenzene), using the method of Cislak and Hamilton [13]. In view of the fact that the amine failed to melt sharply, for further purification it was converted to the acetyl derivative [13], which was then recrystallized several times from acetic acid •• to a constant melting point of 251-253°. The 2-acetylamino-7-nitrofluorene was hydrolyzed by boiling for 5 hours with concentrated hydrochloric acid (as a suspension). The hydrochloride obtained in this manner was dissolved in a large volume of boiling acidulated water and the free amine was precipitated by the addition of ammonia. Then the amine was recrystallized twice from pyridine and 3 times from methanol, m. p. about 229° (in the literature [13, 14], m. p. 229° (cor.) and 221°).

II. Method Used to Measure the Reaction Rate and Results

In an inert solvent the reaction between an aromatic amine and a carboxylic acid chloride proceeds in such a manner that one mole of the chloride combines with two moles of the amine. Consequently, the same as in previous studies [1-4], the solutions were prepared in such manner that the concentration of the chloride (a) in the mixture of reactants was exactly half the concentration of the amine (b).

The method used to measure the reaction rate has been described in detail in a previous communication

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• Balcom and Furst [11], who proposed this general method for the reduction of nitro compounds, recommend running the reaction in ethanol. We found that it also proceeds with equal ease in methanol.

•• As is indicated in the synthesis method [13].

[4]; In essence it is based on the fact that after a predetermined time interval the reaction was terminated by pouring a benzene solution of diethylamine into the reactant mixture, after which the unacylated amine was determined by potentiometric titration with sodium nitrite [15].

The bimolecular rate constant, energy of activation (E), preexpotential term of the Arrhenius equation (PZ) and the entropy of activation ($\Delta S^{\neq}$) were calculated in exactly the same manner as indicated in communication [4].

Practically coinciding results were obtained when the kinetics experiments were repeated after several months with a newly prepared series of aminofluorene samples (a different method was used for their purification).

The numerical data obtained for the reactions studied in the present communication are collected in Tables 1 and 2, where the following designations are used: t_i are the time intervals after which the rate is measured; and k_i and k are respectively the average value of the rate constant: 1) for a given t_i with number of measurements n_i, and 2) for all Σn_i of the measurements. In these tables the average value of the reaction yield for n_i measurements is given in the second column.

TABLE 1

Kinetics For the Reaction of 2-Aminofluorene With p -Nitrobenzoyl Chloride

$$a = 0.00125\ \frac{\text{mole}}{\text{liter}}; \qquad b = 0.0025\ \frac{\text{mole}}{\text{liter}}$$

Temperature 25°				Temperature 50°			
t_i (min.)	Yield (%)	k_i $\left(\frac{\text{liter}}{\text{M} \cdot \text{sec.}}\right)$	n_i	t_i (min.)	Yield (%)	k_i $\left(\frac{\text{liter}}{\text{M} \cdot \text{sec.}}\right)$	n_i
3	33.0	1.10	3	2	40.2	2.32	3
4	40.3	1.13	3	3	50.7	2.37	3
5	45.3	1.11	3	4	57.6	2.35	3
7	53.9	1.12	3	5	62.5	2.30	2
10	62.6	1.12	3	7	70.2	2.32	3
15	71.5	1.12	3				
$K_{25^\circ} = 1.12 \pm 0.01$				$K_{50^\circ} = 2.33 \pm 0.02$			

$$E = 5600\ \frac{\text{cal}}{\text{mole}}; \quad PZ = 1.4 \cdot 10^{4}\ \frac{\text{liter}}{\text{mole} \cdot \text{sec.}} \quad \Delta S^{\neq} = -41.6\ \frac{\text{cal}}{\text{degree} \cdot \text{mole}}$$

The principal data on the kinetics of the reactions studied in the present communication are summarized in Table 3, as are also the values of some of the constants for the reactions studied by us earlier.

Discussion of Results*

2-Aminofluorene (V) and 2-amino-7-nitrofluorene (VI) can be regarded as being analogs, on the one hand, of 4-amino-biphenyl (I) and 4-amino-4'-nitrophenyl (II), and on the other, of the 2,2'-dimethyl derivatives of these amines (III) and (IV). A distinguishing characteristic of each of the mentioned pairs of compounds is the fact that the angle between the planes of the benzene rings is greatest in the case of the dimethyl derivatives of biphenyl,** decreases in the transition to the compounds not substitued in the 2,2'-positions, and is practically nonexistent for the fluorene derivatives.

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* See Table 3.

** See the literature cited in previous communications.

TABLE 2

Kinetics For the Reaction of 2-Amino-7-nitrofluorene With p-Nitrobenzoyl Chloride

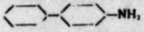
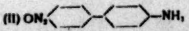
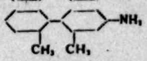
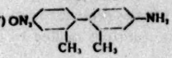
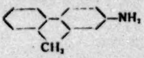
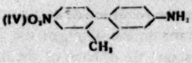
$a = 0.00125 \frac{\text{mole}}{\text{liter}}$; $b = 0.0025 \frac{\text{mole}}{\text{liter}}$

Temperature 25°				Temperature 50°			
t_i(min.)	Yield (%)	k_i $\left(\frac{\text{liter}}{\text{M}\cdot\text{sec.}}\right)$	n_i	t_i(min.)	Yield (%)	k_i $\left(\frac{\text{liter}}{\text{M}\cdot\text{sec.}}\right)$	n_i
10	9.6	0.0712	2	10	17.1	0.142	3
25	20.5	0.0690	3	15	23.2	0.139	5
50	31.2	0.0599	5	25	34.9	0.148	4
80	46.9	0.0739	5	40	44.8	0.140	5
120	57.8	0.0765	5	60	57.2	0.154	2
180	66.4	0.0738	3	90	66.7	0.154	3
$K_{25^\circ} = 0.0727 \pm 0.0031$				$K_{50^\circ} = 0.145 \pm 0.001$			

$E = 5300 \frac{\text{cal}}{\text{mole}}$; $PZ = 5.5 \cdot 10^2 \frac{\text{liter}}{\text{mole}\cdot\text{sec.}}$ $\Delta S^{\parallel} = -48.1 \frac{\text{cal.}}{\text{degree}\cdot\text{mole}}$

TABLE 3

Summarized Data On the Kinetics For the Acylation of Amines With p-Nitrobenzoyl Chloride •

Amine	K_{25°	K_{50°	E	PZ	$\Delta S^{\parallel}$
(I) 	0.533 ± 0.010	1.11 ± 0.02	5600	$7.1 \cdot 10^3$	—42.8
(II) 	0.0505±0.0011	0.118±0.003	6500	$2.9 \cdot 10^3$	—44.7
(III) 	0.792 ±0.028	1.79 ±0.011	6200	$3.0 \cdot 10^4$	—40.1
(IV) 	0.114 ±0.006	0.386±0.016	9300	$7.8 \cdot 10^5$	—33.6
(V) 	1.12 ±0.01	2.33 ±0.02	5600	$1.4 \cdot 10^4$	—41.6
(IV) 	0.0727±0.0031	0.145±0.001	5300	$5.5 \cdot 10^2$	—48.1

•The dimensions of the constants are the same as those given in Tables 1 and 2.

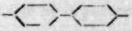
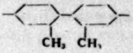
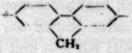
The ratio of the acylation rate constants for each pair of the examined compounds

$$\frac{K_I}{K_{II}} = f_1 ; \quad \frac{K_{III}}{K_{IV}} = f_2 ; \quad \frac{K_V}{K_{VI}} = f_3$$

characterizes the magnitude of the reactivity transmitted by the NO_2 and NH_2 groups respectively: 1) through a system of two benzene rings connected by a simple bond; 2) through a system of the same rings in the presence of steric hindrance, evoked by substituents in the 2,2'-positions, and 3) through a system of the same benzene rings, made additionally stronger by a bridging methylene group. We will call the indicated ratio of the constants the factor for the transmission of electronic reactivity of substituents through a system (f). From the data given in Table 4 it is quite evident that the value of factor f is greatest for the fluorene system and least for the 2,2'-dimethylbiphenyl system, while the unsubstituted biphenyl system occupies an intermediate position. This is in accord with the fact that the arrangement of the planes of the benzene rings in the fluorene molecule is planar, or nearly planar, while in the case of the other two systems the planes of the indicated rings form an angle, in which connection the angle is considerably greater for the 2,2'-derivatives of biphenyl than for the analogous unsubstituted compounds.

TABLE 4

Values of the Factors f For the Biphenyl, 2,2'-Dimethylbiphenyl and Fluorene Systems

System	$f_{25°}$	f_{50}
	10.6	9.41
	6.95	4.64
	15.4	16.1

However from the results obtained by us it follows that in itself the planarity of the molecule always plays a less essential role here than might have been expected, since the value of f for the fluorene system is not very much different from the corresponding value for the biphenyl system, even though the biphenyl molecule is nonplanar, while the fluorene molecule has a planar structure. This fact is a serious argument in support of the situation that a weak conjugation between the benzene rings in the biphenyl molecule is due not only to its nonplanar structure [1, 2], but is also conditioned by the inherent stability shown by the electronic system of the benzene ring [16]. In comparison with the above mentioned geometric considerations, the last circumstance apparently possesses the greater importance. Also not excluded is the probability that the noted comparatively small conductivity shown by the fluorene system with respect to the electronic reactivity of substituents is due to strains, created by the closure of the five-membered ring in the fluorene molecule and its associated shift of the centers of symmetry of the benzene rings to one side of the bond line connecting these rings [6, 7].

The following detail deserves attention. If in its kinetic parameters 2-aminofluorene is similar to its extremely close analog, 4-amino-2,2'-dimethylbiphenyl, then 2-amino-7-nitrofluorene differs sharply in this respect from its analog, 4-amino-4'-nitro-2,2'-dimethylbiphenyl, especially in the values of the energy and entropy of activation. Substantially, however, kinetics data for the acylation of 2-amino-7-nitrofluorene are comparable to similar data for 4-amino-4'-nitrobiphenyl, in which connection the value of E for the fluorene derivative is even lower than the corresponding value for the biphenyl derivative. We hope to give an explanation of this interesting fact in the near future when was discuss the whole problem of the relationship between spatial configuration and reactivity in the series of biphenyl derivatives.

SUMMARY

1. The kinetics of the reaction for the acylation of 2-aminofluorene and 2-amino-7-nitrofluorene with p-nitrobenzoyl chloride in benzene solution was studied.

2. It was shown that the fluorene system, being more planar than the biphenyl system, is a better agent for the transfer of the electronic influences exerted by substituents.

LITERATURE CITED

[1] L. M. Litvinenko and A P. Grekov, Ukrain. Chem. J. 20, 194 (1954).

[2] L. M. Litvinenko and A. P. Grekov, in the book: "Problems of Chemical Kinetics, Catalysis and Reactivity ", p. 860 (1955), Acad. Sci. USSR Press; Trans. Sci.-Res. Inst. Chemistry and Chem. Faculty, Kharkov State Univ., 14, 165 (1956).

[3] L. M. Litvinenko, S. V. Tsukerman and A. P. Grekov, Proc. Acad. Sci. USSR, 101, 265 (1955); Ukrain. Chem. J., 21, 510 (1955).

[4] L. M. Litvinenko and A. P. Grekov, J. Gen. Chem., 26, 3391 (1956).*

[5] A. Kh. Khalilov and P P. Shorygin. Proc. Acad. Sci. USSR, 78, 87 (1951); J. Phys. Chem., 27, 330 (1953).

[6] D. Burns, J. Iball, Nature, 173, 635 (1954).

[7] G. Brown, M. Bortner, Acta crystallogr., 7, 139 (1954); Abst. J. Chem., 1954, No. 20, 44,339.

[8] R. Sandin, R. Melby, A. Hay, R. Jones, E. Miller, J. Miller, J. Am.Chem. Soc., 74, 5073 (1952).

[9] Organic Syntheses, Coll. Vol. II, p. 385 (1949).

[10] L. M. Litvinenko, A P. Grekov, N. N. Verkhovod and V. P. Dzyuba, J. Gen. Chem., 26, 2524 (1956).*

[11] D. Balcom, A Furst, J. Am. Chem. Soc., 75, 4334 (1953).

[12] G. Morgan, R. Thomason, J. Chem. Soc., 1926 , 2693.

[13] F. Cislak, C. Hamilton, J. Am. Chem. Soc., 53, 746 (1931).

[14] B. A. Porai-Koshits. J. Gen. Chem., 14, 1015 (1944).

[15] L. M. Litvinenko and A. P. Grekov, J. Anal. Chem., 10, 164 (1955). (T. p. 153).**

[16] E. A Shilov, Ukrain.Chem. J., 18, 130 (1952).

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*Original Russian pagination. See C.B. translation.

**T.p. = C.B. Translation pagination.

ORIENTATION WITH SUBSTITUTION IN THE AROMATIC SERIES

I. SULFONATION OF m-TOLUENESULFONIC ACID

A. A. Spryskov and T. I. Yakovleva

In substitution in the benzene ring the degree of reactivity of the compound and the reaction conditions, i. e., the temperature, activity of the attacking agent and duration of reaction, exert an influence on the orientation shown by a newly introduced substituent. In the present study, by means of running experiments on the sulfonation of m-toluenesulfonic acid we propose to show the influence exerted by the indicated factors on the orientation of the newly introduced sulfo group.

When substituents of Class I and II are present in m-toluenesulfonic acid, standing meta with respect to each other, there occurs the case of noncoinciding orientation, and consequently, considering it impossible for the sulfo group to enter the benzene ring ortho- to the other, the formation of 1,2,5- and 1,3,5-toluenedisulfonic acids is possible.

Since the degree of influence exerted by substituents is determined by their position in the Holleman series it follows, in accord with the classical orientation rules, that the formation of 1,2,5-toluenedisulfonic acid can be expected.

m-Toluenesulfonic acid had been sulfonated earlier by Klason [1] as the barium salt under heating with 2.5 parts of strongly fuming oleum for 3-4 hours at 180°. For purification the mixture of sulfonic acids was converted into the chlorides. To separate the 1,2,5- and 1,3,5-isomers the chlorides were converted into the barium salts, which for identification purposes were again converted to the acid chlorides. The ratio between the isomers was not established; despite this Klason [2] assumed the 1,2,5-isomer to be the main product.

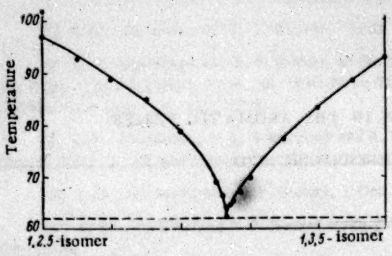
However, our experiments revealed that the 1,3,5-isomer is the predominant product, i.e., the sulfo group enters mainly in the meta-position to the methyl group. This case is outside the scope of the classical rules for orientation in the benzene ring.

The influence of temperature and duration of the process in the sulfonation reaction had also been repeatedly observed earlier, without touching on a change in the type of orientation, since the influence of these factors had been extended to the ratio of the ortho- and para-isomers. Only a few isolated facts exist with respect to a change in the type of orientation.

Thus, Holleman and Caland [3] observed a slight increase in the amount of m-toluenesulfonic acid when the temperature for the sulfonation of toluene was increased, while Olivier [4] observed the formation of 1,3,5-chlorobenzenedisulfonic acid from chlorobenzene at 300° and of 1,3,5-bromobenzenedisulfonic acid from bromobenzene [5].

EXPERIMENTAL

m-Toluenesulfonic acid and its chloride were obtained by the sulfonation of o-toluidine to o-toluidine-5-sulfonic acid [6] with subsequent diazotization and removal of the diazonium group with alcohol. The salt of the m-toluenesulfonic acid was converted to the chloride, which was then vacuum-distilled. The amide obtained from it had m. p. 108°.



Fusion diagram of mixtures of 1,2,5- and 1,3,5-toluenedisulfonyldichlorides.

1,2,5-Toluenedisulfonic acid was also obtained from o-toluidine-5-sulfonic acid by its diazotization and replacement of the diazo group by the disulfide group with the aid of sodium disulfide. The disulfide disulfonic acid was oxidized with permanganate and the salt of 1,2,5-toluenedisulfonic acid was converted to the dichloride, which after recrystallization from benzene melted at 97.1°.

1,3,5-Toluenedisulfonic acid was obtained by the sulfonation of o-toluidine to 2-aminotoluene-3,5-disulfonic acid with subsequent diazotization and removal of the diazo group [7]. The obtained dichloride melted at 93°.

We used pure oleum and distilled chlorosulfonic acid.

To determine the ratio of the formed isomers we used the method of thermal analysis of the binary system 1,2,5- and 1,3,5- toluenedisulfonyl dichlorides. The results of determining the temperatures at which a liquid appeared and the solid phase disappeared for artificially prepared mixtures of the two chlorides are given in Table 1. The determinations were made by the method of heating the mixtures in capillaries with short thermometers. The fusion diagram constructed from these data (see Figure) shows that the chlorides do not form chemical compounds with each other and that the system has a eutectic point, lying at 62° and corresponding to the composition of 46.8% 1,2,5-toluenedisulfonyl dichloride.

In studying the influence of various factors on the orientation of the sulfo group it was also necessary to show which of the two isomers formed here is most stable to the reverse reaction (hydrolysis). For this we ran some experiments in which the pure dichlorides were first heated with a known amount of sulfuric acid of variable concentration at 150° for 5 hours in tubes with a Bunsen seal in order to saponify the chloride and remove the hydrogen chloride. Then the tubes with the 1,2,5- and 1,3,5-isomers were sealed and heated together in a thermostat. The amount of hydrolyzed sulfonic acid was calculated from the increase in the amount of sulfuric acid after hydrolysis, determined gravimetrically as barium sulfate.

TABLE 1

System of 1,2,5- amd 1,3,5-Toluenedisulfonyl Dichloride

Amount of 1,2,5-dichloride (%)	Temperature		Amount of 1,2,5-dichloride (%)	Temperature	
	appearance of liquid phase	disappearance of solid phase		appearance of liquid phase	disappearance of solid phase
0	92.6	93.0	47	63.0	64.3
10	62.0	88.6	48	62.0	66.5
20	62.0	83.5	50	63.0	69.0
30	62.0	77.5	60	62.0	78.8
40	62.0	70.0	70	63.0	85.0
43	62.0	67.2	80	62.0	88.9
45	63.0	65.5	90	62.0	92.8
46	62.0	65.0	100	96.7	97.1

It was conditionally assumed in the calculations that the hydrolysis goes to the monosulfonic acid. The experimental results, presented in Table 2, show that the 1,3,5-disulfonic acid is kinetically more stable to desulfonation than the 1, 2, 5,-isomer. For all practical purposes this toluenedisulfonic acid is not hydrolyzed at 150°. In Expts. 17, 19 and 21 nearly the same amount of the 1,2,5- acid was hydrolyzed with 50, 60 and 70% sulfuric acid. This is explained by the fact that sulfonation of the monosulfonic acid begins in 65-70% acid. Thus, in a special experiment after heating 0.5 g of the m-toluenesulfonyl chloride with 2.5 g of 69% sulfuric acid at 183° for 18 hours it was found that 3% of the sulfuric acid was consumed for sulfonation. As a result, in Expts. 17 and 19 both hydrolysis and sulfonation take place, and consequently, also isomerization with accumulation of the 1,3,5-isomer.

TABLE 2

Hydrolysis of 1,2,5- and 1,3,5-Toluenedisulfonic Acids in the Presence of Sulfuric Acid

Expt. No.	Isomer	Temperature	Duration (hours)	Moles of water taken per mole of disulfonic acid	Concentration of sulfuric acid (%)	Hydrolyzed sulfonic acid (in % of amount taken)
15	1,2,5-	150°	12	8.35	70.5	0
16	1,3,5-	150	12	8.00	70.6	0
17	1,2,5-	183	16	9.90	70.5	28.0
18	1,3,5-	183	16	9.75	70.0	5.2
19	1,2,5-	183	25	7.85	59.8	26.2
20	1;3,5-	183	25	7.55	59.5	2.8
21	1,2,5-	183	16	9.83	49.0	28.6
22	1,3,5-	183	16	9.35	48.6	1.4

To study the influence of the activity of the reagent, the duration of reaction and the temperature on the orientation we ran 3 series of experiments on the sulfonation of m-toluenesulfonic acid.

The experiments were run as follows. The sulfonation agent was added to a known weight of m-toluenesulfonyl chloride in a test tube. The reaction was run for 25 hours and more in sealed test tubes, and in the remaining cases with a Bunsen seal. Then the sulfonic acids in the mixture were converted to the chlorides by treatment with chlorosulfonic acid for 2 hours at room tenperature. The chlorides, isolated by pouring over ice, were filtered, dried over phosphoric anhydride, and then their melting point was determined.

The fusion diagram for the mixtures of the 1,2,5- and 1,3,5- dichlorides has two branches of such a character that nearly each melting point corresponds to two different compositions. Consequently to the investigated mixture of chlorides was added a known weight of either pure 1,2,5- or 1,3,5- dichloride and the melting point of the new mixture was determined. An increase or decrease in the melting points indicated whether the mixture belonged to the right or left branch. The data of these determinations are presented in Table 6.

TABLE 3

Sulfonation of m-Toluenesulfonyl Chloride With Reagents of Different Activity at Room Temperature

Expt. No.	Sulfonation agent and its amount	Monochloride taken	Duration (hours)	M.P. of mixed dichlorides		Composition of mixture (in %)	
				initial	final	1,2,5-	1,3,5-
41	100% H_2SO_4 (9.91 g)	2.02 g	1848*	60°	71.5°	38	62
42	HSO_3Cl (5.0 ml)	0.50 g	324	61	73.0	35	65
43	58% oleum (2.0 ml)	1 ml	48	61	79.0	26	74

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*Since after 1848 hours unsulfonated chloride was still present, then chlorosulfonic acid was added, and the mixture was let stand another 1320 hours, after which it was heated for 40 minutes at 100°.

The results of the first series of sulfonation experiments using sulfonation agents of variable activity, presented in Table 3, show that the more active the agent the greater the amount formed of the stable 1,3,5-isomer with a meta-arrangement of the substituents.

Thus, more of the stable 1,3,5-isomer was obtained in Expt. 41 than in Expt. 40, due to the fact that chlorosulfonic acid is more active than 100% sulfuric acid. The more active oleum gives an even larger amount of the stable 1,3,5-isomer. In these experiments, run at low temperature, the possibility of isomerization through hydrolysis and secondary sulfonation is excluded.

The results of the second series of sulfonation experiments with a variable reaction time, presented in Table 4, show that the amount of the 1, 3, 5-isomer also increases with increase in the duration of the process. In this case isomerization occurs through hydrolysis and secondary sulfonation, leading to an accumulation of the more hydrolysis-resistant isomer.

TABLE 4

Sulfonation at 183° With 100% Sulfuric Acid and a Variable Reaction Time

Expt. No.	Taken		Duration (hours)	Melting point of product		Composition of product (in %)	
	monochloride (g)	monohydrate (g)		initial	final	1,2,5-	1,3,5-
30	0.5786	1.600	4	59°	66.5°	44.0	56.0
31	0.5487	1.733	12	59	73.0	35.5	63.5
32	0.5349	1.729	25	59	78.5	28.5	71.5
36	0.8962	2.773	40	60	82.5	21.5	78.5

TABLE 5

Sulfonation of m-Toluenesulfonyl Chloride at Various Temperatures

Expt. No.	Taken			Temperature	Duration (hours)	Melting point of product		Composition of product (in %)	
	m-toluenesulfonyl chloride (g)	100% H_2SO_4 (g)	60% oleum			initial	final	1,2,5	1,3,5-
26	1.015	2.366		100°	8	59°	64.0°	47	53
27	1.003	2.184		132	8	60	63.6	47	53
40	1.005	2.185		183	8	60	69.0	41	59
43	1 ml		2	20	48	61	79.0	26	74
38	1 ml		2	167—174	4	61	85.5	16	84

The experimental results, presented in Table 5, show the influence of temperature on the ratio of the isomers. To be sure, a mixture of nearly the same composition was obtained in Expts. 26 and 27, since the difference in the sulfonation temperatures was small, and hydrolysis was still absent. An increase in the amount of the 1,3,5-isomer becomes noticeable when the temperature is raised to 183° where hydrolysis occurs, and consequently, isomerization of the sulfonic acid. However, an increase in the sulfonation temperature exerts an influence on the ratio of the isomers even in the absence of hydrolysis, which is the case, for example, when high percent oleum is used. The results of the last two experiments in Table 5 show that the amount of the 1,3,5-isomer changes sharply when the temperature for the sulfonation with 60% oleum is changed from 20 to 170°.

As a result, the temperature is also one of the factors that influence the orientation of the sulfo group.

The results of determining the section on the fusion curve corresponding to the melting points of the obtained dichlorides are given below in Table 6.

When compared with toluene a change in the ortho-, para-orientation to meta-orientation occurs first of all as the result of deactivation of the ring by the sulfo group, shifting the orienting influence toward the meta-isomer, which shows a greater stability to the reverse reaction. As was indicated above, the reaction conditions also exert an important influence. In all of the sulfonation experiments the stable meta-isomer (1,3,5-) is formed in predominant amount, and in some cases its amount reaches 84%.

TABLE 6

Melting Point of Mixed Samples of Dichlorides

Expt. No.	Taken		Calculated composition of the mixture and m.p.				Melting point of mixed sample*
	Investigated dichloride mixture(g)	1,3,5- dichloride(g)	left branch		right branch		
			1,3,5- (%)	melting point*	1,3,5- (%)	melting point*	
30	0.0863	0.0050	54.6	65.2	58.4	69	68.5
31	0.0567	0.0111	56.0	66.3	69.5	77.3	78.0
32	0.0482	0.0200	58.0	68.3	79.7	83.2	83.8
36	0.0754	0.0200	47.4	72.6	83.0	85.0	85.8
38	0.1676	0.0300	38.8	79.5	86.5	86.9	87.0
40	0.0937	0.0100	55.3	66.0	62.4	71.3	71.5
41	0.1303	0.0202	55.5	66.3	67.2	75.6	76.0
42	0.1295	0.0200	53.7	63.3	69.7	77.0	77.0
43	0.1261	0.0200	46.9	73.3	77.7	82.0	82.3

SUMMARY

1. The thermal equilibrium diagram for the binary system composed of the 1,2,5- and 1,3,5-toluenedisulfonyl dichlorides was obtained.

2. The experiments on the hydrolysis of the 1,2,5- and 1,3,5-toluenedisulfonic acids revealed that the 1,3,5-isomer is the more kinetically stable isomer.

3. The ortho-, para-orienting influence of the methyl group in toluene is weakened in m-toluenesulfonic acid due to deactivation of the ring by the sulfo group. The sulfonation of the m-toluenesulfonic acid results in the predominant formation of the more stable meta-isomer (1,3,5-toluenedisulfonic acid).

4. The amount of the stable 1,3,5-isomer is increased with increase in the temperature and activity of the sulfonating agent. An increase in the duration of the process in the presence of conditions conducive for isomerization operates in the same manner.

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*Fixed by the final melting point.

LITERATURE CITED

[1] P. Klason, Ber., 19, 2888 (1886).

[2] P. Klason, Ber., 20, 352 (1887).

[3] A. F. Holleman, P. Caland, Ber., 44, 2504 (1911).

[4] S. C. J. Olivier, Rec. trav. chim., 37, 307 (1918); 38, 351, 356 (1919).

[5] S. C. J. Olivier, K. J.B. Kleermaeker Jr., Rec. trav. chim., 39, 640 (1920).

[6] Organic Syntheses, 4, 477 (1953). Leningrad Press.

[7] M. S. Kisteneva and M. S. Rozhdestvensky, J. Appl. Chem., 22, 1110 (1949).

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TRIAROXYPHOSPHAZOSULFONARYLS AND DIARYL ESTERS OF ARYLSULFONAMIDOPHOSPHORIC ACIDS

A. R. Kirsanov and R. T. Makitra

For the purpose of studying their insecticidal properties we synthesized some triaroxyphosphazosulfonaryls of type $ArSO_2N{=}P(OAr')_3$ and some diaryl esters of the arylsulfonamidophosphoric acids of type $ArSO_2NHPO(OAr')_2$, based on the schemes that we had developed earlier [1], with Ar = phenyl, o- and p-tolyl, and Ar' = o- and p-chlorophenyl and o- and p-nitrophenyl.

The o- and p-trichlorotriphenoxyphosphazosulfonaryls are colorless crystalline substances (with the exception of o-trichlorotriphenoxyphosphazosulfon-p-tolyl, which is liquid at room temperature), of neutral character, insoluble in water, readily soluble in acetone, ethyl acetate and ethyl ether, and crystallizing from ethyl alcohol, petroleum ether and carbon tetrachloride. The para-chloro compounds melt considerably higher and are more difficultly soluble than the corresponding ortho-chloro compounds. When boiled with caustic alkalies in alcohol solution the trichlorotriphenoxyphosphazosulfonaryls are saponified with the formation of the sodium salts of arylsulfonamidophosphoric acid diesters [2]. The diesters are always formed as secondary products in the synthesis of triaroxyphosphazosulfonaryls in yields of 14-37%, and can be obtained in 90-95% yields from the dichlorides of arylsulfonamidophosphoric acids and sodium chlorophenolates. The o- and p-dichlorophenyl esters of the arylsulfonamidophosphoric acids melt considerably above the corresponding trichlorotriphenoxyphosphazosulfonaryls, crystallize well from benzene, are readily soluble in acetone, methyl alcohol, ethyl alcohol and ethyl acetate, represent strong monobasic acids, and with alkalies give salts that crystallize well and are saponified with difficulty by alkalies.

The o- and p-trinitrotriphenoxyphosphazosulfonaryls represent light-yellow crystalline substances of neutral character, readily soluble in dioxane at room temperature, crystallizing from benzene, and insoluble in water and most organic solvents. The para-nitro derivatives melt higher and are considerably more difficultly soluble than the ortho-nitro derivatives. The trinitrotriphenoxyphosphazosulfonaryls are saponified with considerably greater ease than the trichlorotriphenoxyphosphazosulfonaryls. Thus, for example, they are completely saponified to the dinitrodiphenyl esters of arylsulfonamidophosphoric acids when boiled with 95% alcohol in the absence of alkali (see [2]).

The dinitrodiphenyl esters of the arylsulfonamidophosphoric acids represent crystalline substances with a hardly perceptible light-yellow color, readily soluble in alcohol and acetone, very difficultly soluble in water and most organic solvents, crystallizing from aqueous alcohol, and showing the properties of strong monobasic acids. With alkalies they give clearly colored, well-crystallizing salts. With the exception of the di-p-nitrodiphenyl ester of p-tolylsulfonamidophosphoric acid, the diesters melt above the corresponding trinitrotriphenoxyphosphazosulfonaryls (see EXPERIMENTAL).

EXPERIMENTAL

Tri-p-chlorotriphenoxyphosphazosulfonaryls and Di-p-chlorodiphenyl Esters of Arylsulfonamidophosphoric Acids. To a suspension of 0.09 mole of p-chlorophenolate in 50 ml of benzene was added with vigorous stirring a solution of 0.03 mole of the corresponding trichlorophosphazosulfonaryl in 25 ml of benzene. Vigorous reaction began immediately, accompanied by heat-evolution. The phenolate precipitate disappeared, and a slimy precipitate of sodium chloride appeared.

To complete the reaction the mixture was heated at the boil for 30 minutes, then the benzene was vacuum-distilled, and the residue was treated with 100 ml of 0.3N sodium hydroxide solution and thoroughly mixed. Here the tri-p-chlorotriphenoxyphosphazosulfonaryls deposited as colorless, coarsely crystalline precipitates, while the sodium salts of the diesters separated as nearly colorless oils, quite difficultly soluble in water. The phosphazosulfon- compounds were suction-filtered, thoroughly washed with water, and recrystallized from alcohol.

The light-yellow oils of the sodium salts of the diesters, filtered together with water, crystallized on standing. The salts were dissolved in water and the resulting solutions were acidified. The diesters deposited as oils, which soon crystallized completely. For purification they were recrystallized from benzene.

Tri-o-chlorotriphenoxyphosphazosulfonaryls and Di-o-chlorodiphenyl Esters of Arylsulfonamidophosphoric Acids. We were unable to obtain these compounds in the crystalline state by the above-described method. To obtain them it was necessary to start with very pure o-chlorophenolate, completely soluble in ether, and to run the reaction not in benzene, but in ether.

To a solution of 0.06 mole of o-chlorophenolate in 50 ml of ether was added all at once a solution of 0.02 mole of the corresponding trichlorophosphazosulfonaryl in 25 ml of ether and the flask was immediately closed with a reflux condenser. A stormy reaction began immediately, accompanied by boiling of the ether and the separation of sodium chloride as a precipitate. To complete the reaction the mixture was boiled for 15-20 minutes. After cooling, without separating the sodium chloride, the mixture was transferred to a separatory funnel, washed twice with 1N sodium hydroxide solution (20 ml portions), and then 5-8 times with water (10 ml portions) until the wash waters no longer gave either a precipitate or turbidity (diester) when acidified. The ether solution was dried over sodium sulfate and the ether was removed by distillation. The residue contained the tri-o-chlorotriphenoxyphosphazosulfonaryls as viscous light-yellow oils, showing complete crystallization when cooled, with the exception of the tri-o-chlorotriphenoxyphosphazosulfon-p-tolyl, which was a thick viscous liquid.

Acidification of the alkaline wash waters gave a non crystallizing mixture of o-chlorophenol and the corresponding arylsulfonamidophosphoric acid di-o-chlorodiphenyl esters. To isolate the esters the o-chlorophenol was steam-distilled and the solid residue was recrystallized from a mixture of benzene and petroleum ether. We were unable to isolate a crystalline o-tolylsulfonamidophosphoric acid di-o-chlorodiphenyl ester in this manner.

Hydrolysis of Trichlorotriphenoxyphosphazosulfonaryls With Sodium Hydroxide in Alcohol Solution. To a solution of 0.001 mole of trichlorotriphenoxyphosphazosulfonaryl in 10-15 ml of alcohol was added 1.0 ml of 1N sodium hydroxide solution and the mixture was boiled under reflux for 30 minutes, after which the alcohol was distilled off and the residue was treated with 25 ml of water. The clear solution was acidified with hydrochloric acid, and the resulting precipitate of the arylsulfonamidophosphoric acid dichlorodiphenyl ester was suction-filtered, washed, and recrystallized from benzene. The diesters obtained in this manner did not depress the melting points when mixed with specimens of the diesters obtained as secondary products in the synthesis of the trichlorotriphenoxyphosphazosulfonaryls.

Preparation of the Di-o-chlorodiphenyl Ester of Phenylsulfonamidophosphoric Acid From Phenylsulfonamidophosphoryl Dichloride. To 0.09 mole of sodium o-chlorophenolate was added a solution of 0.03 mole of phenylsulfonamidophosphoryl dichloride in 30 ml of benzene. The evolution of heat was observed on mixing. The mixture was boiled under reflux for 30 minutes, then the benzene was vacuum-distilled, the residue dissolved in water, and the solution acidified. To remove the o-chlorophenol the obtained oily substance was steam-distilled until the oil layer turned to a solid crystalline precipitate, which was suction-filtered and washed with water. The yield of the phenylsulfonamidophosphoric acid di-o-chlorodiphenyl ester was 12.8 g (92.7%) (after recrystallization from benzene--prisms with m. p. 149-151°), and it failed to depress the melting point when mixed with the diester obtained by the hydrolysis of tri-o-chlorotriphenoxyphosphazosulfonphenyl.

Trinitrotriphenoxyphosphazosulfonaryls. To 0.06 mole of sodium nitrophenolate, well-dried in vacuo at 140°, was added a solution of 0.02 mole of the corresponding trichlorophosphazosulfonaryl in 150 ml of benzene. A small amount of heat was evolved on mixing.

The reaction mixture was boiled under reflux for 6 hours, to nearly complete disappearance of the red nitrophenolate precipitate, and then the mixture was suction-filtered while boiling hot. Here the o-nitro derivatives remained in the solution, from which they deposited on cooling or after distilling off a part of the solvent. The para-nitro derivatives are much more difficultly soluble in boiling benzene, and for their complete removal it was necessary to extract the precipitate 4-6 times with 150-200 ml portions of boiling benzene. The trinitrotriphenoxyphosphazosulfonaryls, depositing from the benzene solutions, were suction-filtered and washed with benzene, and if necessary, recrystallized from benzene. All of the operations should be carried out in such a manner as to protect the solutions and substances as much as possible from exposure to atmospheric moisture, since the trinitrotriphenoxyphosphazosulfonaryls are saponified with extreme ease.

Dinitrodiphenyl Esters of Arylsulfonamidophosphoric Acids. A mixture of 0.01 mole of the trinitrotriphenoxyphosphazosulfonaryl and 15-30 ml of 95% ethyl alcohol was boiled for 15-20 minutes, water was added to the appearance of turbidity, and the mixture allowed to crystallize. For purification the substance was recrystallized from alcohol or from aqueous alcohol.

The melting points, yields and analysis data for all of the obtained substances are given in Tables 1 and 2.

TABLE 1

Trichlorotriphenoxy- and Trinitrotriphenoxyphosphazosulfonaryls of Type $ArSO_2N=P(OAr')_3$. Obtained by the Scheme

$$ArSO_2N = PCl_3 + 3Ar'ONa \longrightarrow 3NaCl + ArSO_2N = P(OAr')_3$$

Ar	Ar'	Yield (in %)	Melting point	Found % N	Empirical formula	Calculated % N	Yield (in %) $ArSO_2NHPO(OAr')_2$
C_6H_5	$o\text{-}ClC_6H_4$	59.3	72—73°	2.77	$C_{24}H_{17}O_5NCl_3SP$	2.46	14.3
C_6H_5	$p\text{-}ClC_6H_4$	52.7	112—114	2.56	$C_{24}H_{17}O_5NCl_3SP$	2.46	37.8
$o\text{-}CH_3C_6H_4$	$o\text{-}ClC_6H_4$	59.5	73—75	2.75	$C_{25}H_{19}O_5NCl_3SP$	2.40	Not isolated
$o\text{-}CH_3C_6H_4$	$p\text{-}ClC_6H_4$	55.2	121—123	2.32	$C_{25}H_{19}O_5NCl_3SP$	2.40	33.1
$p\text{-}CH_3C_6H_4$	$o\text{-}ClC_6H_4$	52.6	liquid	2.76	$C_{25}H_{19}O_5NCl_3SP$	2.40	16.0
$p\text{-}CH_3C_6H_4$	$p\text{-}ClC_6H_4$	46.9	106—107	2.42	$C_{25}H_{19}O_5NCl_3SP$	2.40	25.4
C_6H_5	$o\text{-}NO_2C_6H_4$	78.8	94—95	c.f. [2]	—	—	Not isolated
C_6H_5	$p\text{-}NO_2C_6H_4$	62.8	123—124	9.51	$C_{24}H_{17}O_{11}N_4SP$	9.33	
$o\text{-}CH_3C_6H_4$	$o\text{-}NO_2C_6H_4$	74.0	151—152	c.f. [2]	—	—	
$o\text{-}CH_3C_6H_4$	$p\text{-}NO_2C_6H_4$	60.5	180—181	9.33	$C_{25}H_{19}O_{11}N_4SP$	9.11	
$p\text{-}CH_3C_6H_4$	$o\text{-}NO_2C_6H_4$	78.7	103—104	9.13	$C_{25}H_{19}O_{11}N_4SP$	9.11	
$p\text{-}CH_3C_6H_4$	$p\text{-}NO_2C_6H_4$	81.4	179—181	9.02	$C_{25}H_{19}O_{11}N_4SP$	9.11	

TABLE 2

Dichlorodiphenyl and Dinitrodiphenyl Esters of Arylsulfonamidophosphoric Acids of Type $ArSO_2NHPO(OAr')_2$, Obtained by the Scheme

$$ArSO_2N{=}P(OAr')_3 + NaOH \rightarrow Ar'OH + ArSO_2NNaPO(OAr')_2$$

Ar	Ar'	Yield (in %)	Melting point	Found % N	Empirical formula	Calculated % N
C_6H_5	o-ClC_6H_4	—*	149—151°	3.12	$C_{18}H_{14}O_5NCl_2SP$	3.06
C_6H_5	p-ClC_6H_4	96.5	155—157	3.05	$C_{18}H_{14}O_5NCl_2SP$	3.06
o-$CH_3C_6H_4$	o-ClC_6H_4	83.4 **	130—132	2.88	$C_{19}H_{16}O_5NCl_2SP$	2.97
o-$CH_3C_6H_4$	p-ClC_6H_4	89.6	139—140	2.88	$C_{19}H_{16}O_5NCl_2SP$	2.97
p-$CH_3C_6H_4$	o-ClC_6H_4	—*	172—174	3.20	$C_{19}H_{16}O_5NCl_2SP$	2.97
p-$CH_3C_6H_4$	p-ClC_6H_4	—*	165—167	3.01	$C_{19}H_{16}O_5NCl_2SP$	2.97
C_6H_5	o-$NO_2C_6H_4$	80.4	150—151	c.f. [2]	—	—
C_6H_5	p-$NO_2C_6H_4$	84.4	199—200	8.75	$C_{18}H_{14}O_9N_3SP$	8.76
o-$CH_3C_6H_4$	o-$NO_2C_6H_4$	66.2	161—162	c.f. [2]	—	—
o-$CH_3C_6H_4$	p-$NO_2C_6H_4$	85.2	189—192	8.42	$C_{19}H_{16}O_9N_3SP$	8.51
p-$CH_3C_6H_4$	o-$NO_2C_6H_4$	88.0	163—164	8.60	$C_{19}H_{16}O_9N_3SP$	8.51
p-$CH_3C_6H_4$	p-$NO_2C_6H_4$	81.2	173—174	8.60	$C_{19}H_{16}O_9N_3SP$	8.51

SUMMARY

For the purpose of studying their insecticidal properties the preparation of twelve chloro- and nitro-substituted triaroxyphosphazosulfonaryls and twelve chloro- and nitro-substituted diaryl esters of arylsulfonamidophosphoric acids was described.

LITERATURE CITED

[1] A. V. Kirsanov and V. I. Shevchenko, J. Gen. Chem., 24, 474, 882 (1954) (T. p. 483, 879).***

[2] A. V. Kirsanov and V. I. Shevehenko, J. Gen. Chem. 24, 1980 (1954). (T. p. 1949).***

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Institute of Organic Chemistry
Academy of Sciences of the
Ukrainian SSR

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* Obtained as a by-product in the synthesis of the corresponding trichlorotriphenoxyphosphazosulfonaryl.

** To isolate the o-tolylsulfonamidophosphoric acid o-dichlorodiphenyl ester it was necessary to first steam-distill the o-chlorophenol, since the o-chlorophenol makes crystallization of the diester exceedingly difficult.

*** T.p. = C.B. Translation pagination.

REACTION OF β-CHLOROVINYL KETONES WITH β-DICARBONYL COMPOUNDS

III. OXOVINYLATION OF MALONIC ESTER. A NEW SYNTHESIS OF α-PYRONES

N. K. Kochetkov and L. I. Kudryashov

In the previous paper [1] we communicated on a new reaction — the reaction of β-chlorovinyl ketones with monoalkylmalonic esters, leading to the formation of β-oxoalkenylmalonic esters. It was natural to make an attempt to extend this interesting and synthetically important reaction to other β-dicarbonyl compounds, and first of all to malonic ester. The distinguishing characteristic in this case was the presence of two active hydrogens, capable of being replaced by the oxovinyl radical. As was shown in our earlier communications [1, 2], this circumstance strongly complicated matters, since it could lead to a complex mixture of substances due to the bisoxovinylation process, which is evidently associated with metallation of the originally formed monooxovinyl derivative by sodiomalonic ester. Actually, the experiments on the reaction of sodiomalonic ester with β-chlorovinyl ketones under the usual conditions of the malonic synthesis (in alcohol or in benzene) failed to give a positive result; we were unable to isolate any individual substances from the obtained complex mixture of reaction products. Such negative results were also obtained by other authors [3].

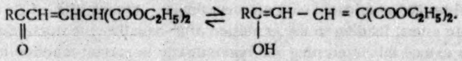
In order to avoid the over-metallation process and keep the reaction at the stage of forming the monooxovinyl derivative in which we were interested, instead of the sodiomalonic ester, we used in the reaction with β-chlorovinyl ketones the corresponding magnesium derivative — ethoxymagnesiummalonic ester, used at the present time for the acylation of malonic ester with acid chlorides. Actually, here we obtained positive results and a general method for the oxovinylation of malonic ester was developed, which permitted us to obtain β-oxoalkenylmalonic esters of type $RCOCH{=}CHCH(COOC_2H_5)_2$, not containing a second substituent in the malonic ester radical. The obtained result again supports the close analogy in the behavior of the β-chlorovinyl ketones and acid chlorides, repeatedly run by us earlier [4]. The reaction proceeds by the general scheme:

$$RCOCH{=}CHCl + C_2H_5OMgCH(COOC_2H_5)_2 \rightarrow RCOCH{=}CHCH(COOC_2H_5)_2.$$
$$(R = CH_3,\ C_2H_5,\ C_3H_7.)$$

The most satisfactory results are obtained when operating under the following conditions. A mixture of malonic ester and magnesium is heated in alcohol solution in the presence of traces of iodine or with a small amount of carbon tetrachloride, with simultaneous removal of the alcohol by distillation; the ethoxymagnesiummalonic ester, remaining after removal of the alcohol, is dissolved in dry benzene, and then the β-chlorovinyl ketone is added in one portion to the cooled solution. The mixture is shaken vigorously with simultaneous cooling and on conclusion of reaction is hydrolyzed with the minimum amount of dilute hydrochloric acid, after which the β-oxoalkenylmalonic ester is isolated by distillation. Such a method of operation gives better results than when the β-chlorovinyl ketone is added gradually to the solution of the ethoxymagnesium malonic ester with stirring, since in the latter case the magnesium derivative of the condensation product separates as a sticky mass, which makes further reaction difficult, and it fails to go to completion.

The essential moment for success of the synthesis is the final operation — the purification of the β-oxoalkenylmalonic esters. It was revealed that these compounds, in contrast to their analogs, not containing hydrogen in the malonic ester radical of type RCOCH=CHCR' $(COOC_2H_5)_2$ [1], are cyclized with great ease to α-pyrone derivatives (see below), in which connection this cyclization proceeds with exceptional ease in the presence of traces of acids. Here it is interesting to mention that in the reaction of methyl β-isopropoxyvinyl ketone with malonic ester Hills and McQuillin [5] obtained in small yield a mixture of β-oxobutenylmalonic ester and 6-methyl-3-carbethoxy-α-pyrone. For successful isolation of completely pure β-oxoalkenylmalonic esters of type $RCOCH = CHCH(COOC_2H_5)_2$ it is necessary to wash out very thoroughly all traces of acid after hydrolysis of the reaction mixture and to distill the substances at the lowest temperature possible, i. e., in a good vacuum. When these conditions are observed the β-oxoalkenylmalonic esters can be obtained in high yields (60-70%) and then can find interesting use for the synthesis of various difficultly accessible aliphatic compounds. We obtained 3-oxobuten-1-ylmalonic, 3-oxopenten-1-ylmalonic and 3-oxohexen-1-ylmalonic esters in this manner.

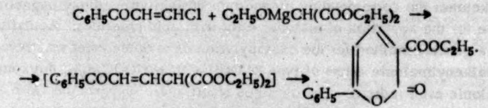
The obtained substances are either colorless or slightly colored liquids, proving to be quite stable to storage. They give the characteristic cherry-red color with alcoholic ferric chloride solution, inherent to enols. The latter can be explained if the presence of keto-enol tautomerism is assumed for the compounds:



$$\underset{\overset{\|}{O}}{RC}CH{=}CHCH(COOC_2H_5)_2 \rightleftharpoons \underset{\overset{|}{OH}}{RC}{=}CH-CH = C(COOC_2H_5)_2.$$

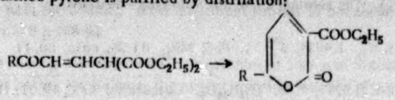
Such an assumption seems to be sufficiently well-based, since the obtained substances are vinylogs of β-oxo acids, and this theoretically important problem is being studied at the present time. It is quite possible that the sticky mass, obtained in the reaction of a β-chlorovinyl ketone with malonic ester, is the magnesium derivative of the enolic form of the reaction product, which is decomposed during hydrolysis.

We were unable to obtain the corresponding aromatic derivative β-benzoylvinylmalonic ester – in analytically pure form by the condensation of phenyl β-chlorovinyl ketone with malonic ester. Despite repeated attempts and observance of all of the precautions (vacuum-distillation at 0.01 mm), the reaction product always contained a substantial amount of 6-phenyl-3-carbethoxy-α-pyrone, which appears as the sole reaction product if the distillation is run at ordinary vacuum (0.1-1 mm).


$C_6H_5COCH{=}CHCl + C_2H_5OMgCH(COOC_2H_5)_2 \rightarrow$
$\rightarrow [C_6H_5COCH{=}CHCH(COOC_2H_5)_2] \rightarrow$
$COOC_2H_5$.
C_6H_5
O
=O

Since up to now sufficiently convenient synthesis methods for the preparation of α-pyrone derivatives have failed to exist, and since compounds of this type could prove to be of pharmacological interest, we made a detailed study of the problem of cyclization of β-oxoalkenylmalonic esters to 6-substituted 3-carbethoxy-α-pyrones and developed a convenient preparative method for their synthesis. It was revealed that this cyclization can be achieved by simple heating, although here the yields of the α-pyrones are small. In this connection it is necessary to mention that repeated distillation of the β-oxoalkenylmalonic esters, even in high vacuum, results in their partial cyclization to pyrones, and consequently additional purification of these esters by repeated distillation is meaningless. However, as yet thermal cyclization cannot be regarded as being a convenient preparative method for obtaining α-pyrones, with the exception of 6-phenyl-3-carbethoxy-α-pyrone, which is obtained most conveniently by this specific method (see above). To completely convert the other oxoalkenylmalonic esters to the pyrones it is necessary to distill them 2 and 3 times in a vacuum of 5-7 mm.

It is more convenient to use acid condensation agents for the cyclization, at times with simultaneous removal of the alcohol by distillation. The condensation agents tested by us included zinc chloride, p-toluenesulfonic acid, hydrochloric acid, sulfuric acid and acetyl chloride. All of the reagents, with the exception of zinc chloride, assure cyclization; however, in the presence of p-toluenesulfonic acid and hydrochloric acid the yields are lower. The use of zinc chloride failed to give positive results. Sulfuric acid gives the pyrones in high yield; however, the obtained substance requires special purification, since here partial saponification of the carbethoxy group in the obtained pyrone and some other secondary processes evidently proceed at the same time. The most suitable condensation agent proved to be acetyl chloride, which also possesses the additional advantage of assuring a homogeneous reaction medium. In this case cyclization is accomplished by the simple heating of a mixutre of the oxoalkenylmalonic ester with acetyl chloride, after which the obtained pyrone is purified by distillation:



$R = CH_3, C_2H_5, C_3H_7.$

In this manner we obtained the 6-methyl-, 6-ethyl-and 6-propyl-3-carbethoxy-α-pyrones in 60-90% yields. The obtained 3-carbethoxy- α-pyrones are either colorless liquids or low-melting solids (methyl and phenyl derivatives), completely stable to storage, soluble in acids, and unstable toward alkalies.

The alkyl-3-carbethoxy-α-pyrones can also be obtained by the direct cyclization of the reaction product of β-chlorovinyl ketones with malonic ester without its previous purification; however, the yields in this case are small, and purification of the substance is difficult, for which reason this synthesis variation is of little value.

As a result, the reaction for the oxovinylation of malonic ester is of interest for developing new methods of organic synthesis in both the aliphatic series and the oxygen-containing heterocyclic series.

EXPERIMENTAL

3-Oxobutenylmalonic Ester. In a flask, connected to a reflux condenser with calcium chloride tube, was placed 4.8 g of magnesium, an iodine crystal was added, the mixture heated to the appearance of iodine vapors, 25 ml of anhydrous alcohol and 31.8 g of malonic ester added through the condenser, and the reaction mixture heated nearly to the boil, avoiding stirring until vigorous reaction had set in (30-45 minutes). If the magnesium fails to go into solution, then another iodine crystal should be added, heating should be discontinued, the mixture allowed to stand without stirring for 1-1.5 hours, and then heated as indicated above. After the main magnesium mass had dissolved (the reaction rate is regulated by cooling), 75 ml of anhydrous alcohol was added, the mixture boiled until all of the magnesium had dissolved, and the alcohol distilled off, the last traces of which were removed by heating in vacuo ; the residue was dissolved in 100 ml of anhydrous benzene, cooled to -10°, a cooled solution of 15.7 g of methyl β-chlorovinyl ketone in 100 ml of anhydrous benzene added as rapidly as possible, and the flask shaken vigorously with simultaneous cooling in an ice water bath. After 15 minutes self-heating had ceased, the flask contents solidified, and after 30 minutes a light-yellow precipitate, gradually turning dark, began to separate. The reaction mixture was allowed to stand overnight, then 100 ml of water was added and slowly with shaking, avoiding self-heating, about 25 ml of concentrated hydrochloric acid, until the precipitate had completely dissolved (about 1.5 hours was required to obtain solution). The benzene layer was separated, washed with water (twice with 30 ml portions), the water extracts extracted with ether (twice with 50 ml portions), the combined ether-benzene extracts treated with fused magnesium sulfate and aluminum oxide, after 2 hours the solvent vacuum-distilled from the filtered solution, and the residue distilled, collecting the fraction with b. p. 119-123° (2 mm), yield 23.8 g (69.6%). The substance has the following constants :

B. p. 121–122° (3 mm), n_D^{20} 1.4646, d_4^{20} 1.1086, MR_D 56.88; calc. 55.85.

Found %: C 57.56, 57.70; H 7.04, 7.04. $C_{11}H_{16}O_5$. Calculated %: C 57.88; H 7.07.

Literature [5]: B. p. 105° (0.1 mm), n_D^{20} 1.4781.

The substance is a pale yellow liquid, and gives an intense violet color with an alcohol solution of ferric chloride; when vacuum-distilled above 3-4 mm it is converted into 6-methyl-3-carbethoxy-α-pyrone.

3-Oxopenten-1-ylmalonic Ester. Obtained under the same conditions as above from 6 g of magnesium, 40 g of malonic ester and 23.7 g of ethyl β-chlorovinyl ketone, using 125 ml of anhydrous alcohol and 125 ml of anhydrous benzene. On distillation the fraction with b. p. 129-136° (2 mm) was collected, yield 21.3 g (44 %). The substance has the following constants:

B. p. 130–134° (2 mm), n_D^{20} 1.4611, d_4^{20} 1.0856, MR_D 61.25, calc. 60.47.

Found %: C 59.07, 59.30; H 7.67, 7.69. $C_{12}H_{18}O_5$. Calculated %: C 59.51; H 7.49.

The substance is a yellowish liquid, and gives an intense cherry-red color with ferric chloride, and easily cleaves alcohol when distilled.

3-Oxohexen-1-ylmalonic Ester. Obtained under the same conditions from 6 g of magnesium, 40 g of malonic ester and 26 g of propyl β-chlorovinyl ketone, using 125 ml of anhydrous alcohol and 125 ml of anhydrous benzene. On distillation the fraction with b. p. 90-93° (0.06 mm) was collected; yield 30.6 g (63 %). The substance has the following constants:

B. p. 90–93° (0.06 mm), n_D^{20} 1.4581, d_4^{20} 1.0494, MR_D 65.39; calc. 65.09.

Found %: C 60.77, 60.55; H 7.96, 7.82. $C_{13}H_{20}O_5$. Calculated %: C 60.92; H 7.87.

The substance is a yellowish liquid, gives an intense cherry-red color with alcoholic ferric chloride solution, and cannot be distilled without change at pressures above 1 mm.

6-Phenyl-3-carbethoxy-α-pyrone. The reaction of 6 g of magnesium, 40 g of malonic ester and 33.3 g of phenyl β-chlorovinyl ketone [6]was run under the conditions described above (125 ml alcohol, 150 ml benzene). On distillation, accompanied by decomposition, a wide fraction with b. p. 150-220° (2-30 mm) was collected. The substance crystallized in the receiver. The crystals were separated and recrystallized from a mixture of benzene and petroleum ether, yield 16.7 g (34.2 %), m. p. 106-106.5°.

Found %: C 68.76, 69.08; H 5.17, 5.00. $C_{14}H_{12}O_4$. Calculated %: C 68.84; H 4.95.

Literature: m. p. 105–106° [7], 105.5–106.5° [8].

6-Phenyl-3-carbethoxy-α-pyrone was obtained as handsome yellow needles, soluble in alcohol, ether and glacial acetic acid, and insoluble in water and petroleum ether.

6-Methyl-3-carbethoxy-α-pyrone. A. A mixture of 6.47 g of 3-oxobutenylmalonic ester and 5 ml of acetyl chloride was boiled for 2 hours in a flask under reflux. The solution after cooling was diluted with petroleum ether, the crystals filtered, dried in vacuo over paraffin, and recrystallized from water; yield 2.7 g (53 %), m. p. 86°.

Found %: C 59.24, 59.19; H 5.30, 5.46. $C_9H_{10}O_4$. Calculated %: C 59.34; H 5.53.

Literature [5]: m. p. 87°.

6-Methyl-3-carbethoxy-α-pyrone was obtained as colorless crystals, readily soluble in benzene, ether and alcohol, soluble in hot water, difficultly soluble in cold water, and insoluble in petroleum ether.

B. A mixture of 13.5 g of the 3-oxobutenylmalonic ester and a crystal of p-toluenesulfonic acid was slowly heated in a distillation flask to 210°, in which connection 1.7 ml of alcohol was removed by distillation. The residue in the flask was cooled, diluted with petroleum ether, the crystals filtered, and then vacuum-dried. The yield of 6-methyl-3-carbethoxy-α-pyrone was 4.1 g (38.3 %).

C. A mixture of 6.2 g of 3-oxobutenylmalonic ester and 5 drops of concentrated hydrochloric acid was heated for 30 minutes on the boiling water bath, after cooling diluted with petroleum ether, the precipitate filtered, and dried. Yield of 6-methyl-3-carbethoxy-α-pyrone 2.36 g (48 %).

D. A mixture of 7.01 g of 3-oxobutenylmalonic ester and 5 drops of concentrated sulfuric acid was heated on the boiling water bath for 2 hours. After treatment similar to the above the yield of 6-methyl-3-carbethoxy-α-pyrone was 3.8 g (68 %).

6-Ethyl-3-carbethoxy-α-pyrone. A mixture of 16.2 g of 3-oxopentenylmalonic ester and 15 ml of acetyl chloride was boiled for 2 hours, the acetyl chloride distilled off, and the residue vacuum-distilled; yield 12.6 g (92%).

M. p. 162-163° (7 mm), n_D^{20} 1.5265, d_4^{20} 1.1767.

Found %: C 60.95, 60.88; H 6.38, 6.40. $C_{10}H_{12}O_4$. Calculated %: C 61.21; H 6.17.

The substance is a colorless liquid, and is miscible with the ordinary organic solvents.

6-Propyl-3-carbethoxy-α-pyrone. A mixture of 15.1 g of 3-oxohexenylmalonic ester and 10 ml of acetyl chloride was boiled for 2 hours, the acetyl chloride distilled off, and the residue vacuum-distilled; yield 8.6 g (68%).

B. p. 164–166° (6 mm); n_D^{20} 1.5770; d_4^{20} 1.1285.

Found %: C 62.88, 62.95; H 6.83 6.88. $C_{11}H_{14}O_4$. Calculated %: C 62.84, H 6.71.

The substance is a colorless liquid, and is miscible with the ordinary organic solvents.

SUMMARY

1. A method was developed for the synthesis of β-oxoalkenylmalonic esters of type $RCOCH{=}CHCH(COOC_2H_5)_2$ by the reaction of β-chlorovinyl ketones with ethoxymagnesiummalonic ester (in 60-70% yields).

2. It was shown that in the presence of acid reagents the β-oxoalkenylmalonic esters of type

$$RCOCH{=}CHCH(COOC_2H_5)_2$$

give in high yield the 6-alkyl-3-carbethoxy-α-pyrones, which can serve as a convenient method for their synthesis.

LITERATURE CITED

[1] N. K. Kochetkov and L. I. Kudryashov, J. Gen. Chem., 26, 851 (1956).*

[2] N. K. Kochetkov, L. I. Kudryashov and A. N. Nesmeyanov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 809, (1955).*

[3] L. Panizzi, Gazz., 77, 549 (1948).

[4] N. K. Kochetkov, Prog. Chem., 24, 32 (1955).

[5] P. R. Hills and F. J. McQuillin, J. Chem. Soc., 1953, 4060.

[6] N. K. Kochetkov, A. Ya. Khorlin and M. Ya. Karpeisky, J. Gen. Chem., 26, 595 (1956).*

[7] I. Walker, J. Chem. Soc., 1939, 120.

[8] N. K. Kochetkov and A. Ya. Khorlin, J. Gen. Chem., 26, 3430 (1956).*

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Institute of Pharmacology and Chemotherapy
Academy of Medical Sciences of the USSR

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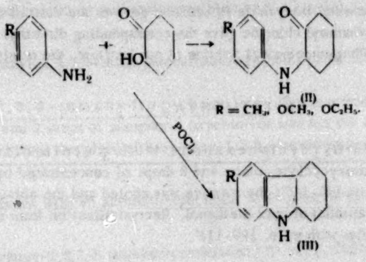
INDOLE DERIVATIVES

III. SYNTHESIS OF 6-HYDROXY-1,2,3,4-TETRAHYDROCARBAZOLE DERIVATIVES

N. K. Kochetkov, N. F. Kucherova and V. P. Evdakov

A large number of physiologically active substances are found in the class of indole derivatives. Eserine, showing strong miotic activity, occupies a prominent position in their number. It is known at the present time that the physiological activity of eserine is associated with the presence of a methyl urethane grouping in it [1]. With the purpose in mind of elucidating the influence of changes in the nucleus of the molecule on the activity, we synthesized the tetrahydrocarbazole analog of eserine, namely the methyl urethane of 6-hydroxy-9-methyl-1,2,3,4-tetrahydrocarbazole (I).

We first attempted to obtain the necessary intermediate–the corresponding hydroxy derivative – by using the method recently proposed by Tomlinson [2] for the synthesis of the tetrahydrocarbazole nucleus, involving the condensation of aromatic amines with 2-hydroxycyclohexanone. For this we studied the condensation of the latter with p-anisidine; however, under the conditions described by Tomlinson we failed to obtain positive results. In this connection we devoted some time to an elucidation of whether the Tomlinson method was suitable for the synthesis of tetrahydrocarbazole derivatives in general. The authors recommend running the reaction under the conditions of heating the amine with the hydroxycyclohexanone in the presence of small amounts of hydrochloric acid; then the tetrahydrocarbazole derivatives should be formed. When we ran this condensation with p-toluidine, p-anisidine and p-phenetidine the properties of the reaction products isolated by us from the reaction mixture did not correspond to the properties of tetrahydrocarbazole derivatives. A study of the obtained substances revealed that they are noncyclic condensation products, and namely 2-arylaminocyclohexanones (II).

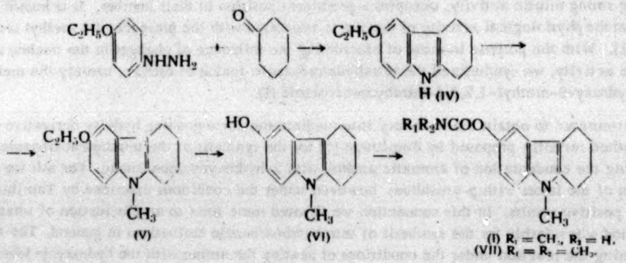


Such a decision as to their structure was supported by the fact that they form hydrazones, and when hydrolyzed with dilute hydrochloric acid they revert back to the aromatic amine and hydroxycyclohexanone.

As a result, the Tomlinson method in the form given by the authors is unsuitable for the synthesis of tetrahydrocarbazoles. Similar conclusions are to be found in a recent paper by some British authors [3], and also in the last paper of Tomlinson himself [4].

Nevertheless, the condensation of aromatic amines with hydroxycyclohexanone to give tetrahydrocarbazole derivatives can be accomplished if the hydrochloric acid, recommended by the indicated author as the condensing agent, is replaced by phosphorus oxychloride. In this case, if the reaction is run at 150-160°, using the necessary amount of oxychloride, the tetrahydrocarbazole derivatives (III) can be isolated. However, the yields of the latter are small (10-30%) and fluctuate from experiment to experiment, for which reason this method can hardly possess preparative significance.

In view of our unsuccessful attempt to obtain the needed 6-hydroxy-9-methyl-1,2,3,4-tetrahydrocarbazole through the hydroxycyclohexanone, we selected a different route for its synthesis. This compound was obtained using the earlier known Fischer-Borsche reaction, and then was converted into our needed methyl urethane by the scheme:



(I) $R_1 = CH_3$, $R_2 = H$.
(VII) $R_1 = R_2 = CH_3$.

The condensation of p-ethoxyphenylhydrazine with cyclohexanone in the presence of sulfuric acid gave 6-ethoxy-1,2,3,4-tetrahydrocarbazole (IV), which when reacted with methyl iodide in acetone was converted to the 9-methyl derivative (V). The latter was saponified by treatment with concentrated hydrobromic acid at elevated temperature. It is interesting to mention that here the hydroxy derivative (VI) separated first as the hydrobromide. Salts of tetrahydrocarbazole are practically unknown, and the formation of such a salt in the given case was evidently the result of the drastic reaction conditions employed. Treatment of the phenol (VI) with methyl isocyanate in benzene gave us the desired methyl urethane (I). Treatment of (VI) with dimethylcarbamoyl chloride gave the corresponding dimethyl urethane (VII). Both compounds are being tested in the Pharmacological Section of our Institute, the results of which will be communicated in another place.

EXPERIMENTAL

Condensation of 2-Hydroxycyclohexanone With p-Toluidine. A mixture of 10 g of p-toluidine, 10.6 g of 2-hydroxycyclohexanone and 2 drops of concentrated hydrochloric acid was heated for 5 minutes in an oil bath at 145-155°; the mixture was cooled and the obtained crystalline substance was washed with a small amount of cold methanol. Recrystallization from methanol gave 9.4 g (50%) of substance as colorless needles with m. p. 109-111°.

Found %: N 7.14, 7.00. $C_{13}H_{17}ON$. Calculated %: N 6.89.

The compound is readily soluble in benzene and ether, and difficultly soluble in alcohol.

The Phenylhydrazone was obtained from 1 g of substance and 0.57 g of phenylhydrazine with heating for 30 minutes on the boiling water bath. The crystalline substance was filtered, and after recrystallization from alcohol a colorless substance with m. p. 96-98° was obtained.

Found %: N 14.27, 14.36. $C_{19}H_{23}N_3$. Calculated %: N 14.24.

Hydrolysis. Two grams of the condensation product in 20 ml of 20% hydrochloric acid was boiled for 30 minutes, cooled, made alkaline with soda, extracted twice with ether, the ether extracts dried over sodium sulfate, dry hydrogen chloride passed into the ether extract, and the crystals filtered. We obtained 1.3 g (92%) of substance with m. p. 234-236°, failing to depress the melting point when mixed with p-toluidine hydrochloride.

Condensation of p-Anisidine With 2-Hydroxycyclohexanone. A mixture of 10 g of p-anisidine, 9.26 g of 2-hydroxycyclohexanone and 2 drops of concentrated hydrochloric acid was heated in an oil bath for 8 minutes at 145-165°. The obtained substance was recrystallized from methanol, and then from ethyl acetate, to give 5.5 g (30%) of substance as plates with m. p. 104-105°.

Found %: C 71.36, 71.40; H 6.70, 6.56; N 6.70, 6.56. $C_{13}H_{17}O_2N$. Calculated %: C 71.20; H 7.81; N 7.81.

The Phenylhydrazone was obtained in the same manner as above; after recrystallization from alcohol it was obtained as yellow crystals with m. p. 124-125°.

Found %: N 13.51, 13.37. $C_{19}H_{22}ON_3$. Calculated %: N 13.63.

Hydrolysis of 1 g of the condensation product by the above-described method gave 0.8 g (72%) of p-anisidine.

6-Methyl-1,2,3, 4-tetrahydrocarbazole. A mixture of 2.15 g of the hydroxycyclohexanone, 2 g of p-toluidine and 2 drops of phosphorus oxychloride was heated for 10 minutes in an oil bath at 150-160°, cooled, the crystals filtered, and after recrystallization from methanol 1.31 g (34%) of substance was obtained as colorless needles with m. p. 142-143°. Its mixed melting point with an authentic specimen of 6-methyl-1,2,3,4-tetrahydrocarbazole was not depressed.

Literature for 6-methyl-1,2,3,4-tetrahydrocarbazole [5]: m. p. 141-142°.

8-Methyl-1,2,3,4-tetrahydrocarbazole. The reaction of 2.15 g of the hydroxycyclohexanone with 2 g of o-toluidine and 2 drops of phosphorus oxychloride was run as indicated above; after the usual treatment and recrystallization from methanol the yield of 8-methyl-1,2,3,4-tetrahydrocarbazole was 1.3 g (34%), m. p. 94-96°.

Its mixed melting point with an authentic specimen of 8-methyl-1,2,3,4-tetrahydrocarbazole was not depressed.

Literature for 8-methyl-1,2,3,4-tetrahydrocarbazole [6]: m. p. 98°.

8-Carboxy-1,2,3,4-tetrahydrocarbazole. The reaction of 2 g of the hydroxycyclohexanone, 2.4 g of anthranilic acid and 2 drops of phosphorus oxychloride was run the same as indicated above; after recrystallization from methanol the yield of 8-carboxy-1,2,3,4-tetrahydrocarbazole was 0.7 g (18%), m. p. 196-198°.

Its mixed melting point with an authentic specimen of 8-carboxy-1,2,3,4-tetrahydrocarbazole was not depressed.

Literature for 8-carboxy-1,2,3,4-tetrahydrocarbazole [7]: m. p. 200-201°.

6-Ethoxy-1,2,3,4-tetrahydrocarbazole. A mixture of 23.5 g of p-ethoxyphenylhydrazine [8] and 15.6 g of cyclohexanone was cautiously heated on the boiling water bath for 3-5 minutes, then 350 ml of dilute sulfuric acid (1:9) was added, and the reaction mixture was boiled for 1 hour. The substance separating after cooling was recrystallized from aqueous methanol (1:1) to give 22.5 g (63%) of substance with

m. p. 102-103.5°.

Literature for 6-ethoxy-1,2,3,4-tetrahydrocarbazole [8]: m. p. 102-104°.

6-Ethoxy-9-methyl-1,2,3,4-tetrahydrocarbazole. A mixture of 15 g of 6-ethoxy-1,2,3,4-tetrahydrocarbazole in 75 ml of acetone, 45 g of potassium hydroxide as 66% solution, and 45 g of methyl iodide was heated with vigorous stirring at the boil for 2 hours. The reaction mass was poured into water, and the crystals were filtered. Recrystallization from methanol gave 13 g (82%) of substance, crystallizing as yellow plates with m. p. 89-90°.

Found %: N 6.30, 6.40. $C_{15}H_{19}ON$. Calculated %: N 6.11.

6-Hydroxy-9-methyl-1,2,3,4-tetrahydrocarbazole. 1 g of 9-methyl-6-ethoxy-1,2,3,4-tetrahydrocarbazole and 5 ml of concentrated hydrobromic acid (d 1.47) was heated in a sealed ampul in an oil bath at 160-165° for 2 hours. Then the hydrobromic acid was vacuum-distilled; the residue was dissolved in anhydrous alcohol, ether was added, and the substance separating as an oil rapidly crystallized. The crystals of the hydrobromide were filtered, m. p. 176-177° (with decompn.). Yield 1.1 g. The hydrobromide was treated with an alcohol solution of 0.22 g of potassium hydroxide. The potassium bromide precipitate was filtered, and the alcohol solution was treated with an equal volume of water. On standing 0.53 g of substance crystallized, which after two recrystallizations from aqueous methanol (1:1) had m. p. 101-102°.

Found %: N 6.74, 6.85. $C_{13}H_{15}ON$. Calculated %: N 6.96.

6-Hydroxy-9-methyl-1,2,3,4-tetrahydrocarbazole Methyl Urethane. A mixture of 2 g of 6-hydroxy-9-methyl-1,2,3,4-tetrahydrocarbazole in 15 ml of anhydrous benzene, 1-2 mg of sodium and 2 g of methyl isocyanate [9] in 6 ml of anhydrous benzene was let stand at room temperature for three days. The precipitate obtained after standing was filtered, and after two recrystallizations from anhydrous alcohol we obtained 1.9 g (74%) of substance as colorless needles with m. p. 167-168°.

Found %: C 69.93, 70.08; H 7.11, 7.15; N 10.64, 10.85, $C_{15}H_{18}O_2N_2$. Calculated %: C 69.70; H 7.02; N 10.84.

6-Hydroxy-9-methyl-1,2,3,4-tetrahydrocarbazole Dimethyl Urethane. A mixture of 0.5 g of 6-hydroxy-9-methyl-1,2,3,4-tetrahydrocarbazole and 1.5 g of dimethylcarbamoyl chloride [10] in 5 ml of pyridine was heated for 3 hours in an oil bath at 140-145°; the reaction mixture was evaporated in vacuo to dryness, treated twice with 10 ml portions of water, and again evaporated in vacuo. The residue was treated with 20 ml of 10% potassium hydroxide solution and extracted three times with ether. The ether extracts were dried over sodium sulfate, and the ether was removed by distillation. The obtained yellow crystalline substance was recrystallized from methanol to give 0.3 g (44%) of substance as yellow needles with m. p. 151-153°.

Found %: C 70.84, 70.18; H 7.57, 7.32; N 10.32, 10.34. $C_{16}H_{20}O_2N_2$. Calculated %: C 70.76; H 7.40; N 10.28.

SUMMARY

1. Two substituted urethane derivatives of 6-hydroxy-9-methyl-1,2,3,4-tetrahydrocarbazole, analogs of eserine in the tetrahydrocarbazole series, were obtained.

2. It was shown that the condensation of aromatic amines with 2-hydroxycyclohexanone in the presence of hydrochloric acid does not yield tetrahydrocarbazole derivatives. Instead the corresponding 2-arylaminocyclohexanones are obtained. The tetrahydrocarbazole derivatives can be obtained in small yields if phosphorus oxychloride is used as the condensing agent in this reaction.

LITERATURE CITED

[1] E. Stedman, Biochem. J., 20, 719 (1926).

[2] O. Janes, M. Tomlinson, J. Chem. Soc. 1953, 4114.

[3] P. Carter, A. Katritzky, S. Plant, J. Chem. Soc., 1955, 338.

[4] J. Cummins, M. Tomlinson, J. Chem. Soc., 1955, 3475.

[5] W. Borsche, Lieb. Ann., 359, 62 (1908).

[6] German Patent 374,098; Chem. Zentr., 1923, IV, 724.

[7] N. Campbell, M. Call, J. Chem. Soc., 1950, 2870.

[8] B. M. Barclay, N. Campbell, J. Chem. Soc., 1945, 530.

[9] G. Colucci, Can. J. Res., 23B, 111 (1945).

[10] Hantzsch, Lieb. Ann., 299, 85 (1898).

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Institute of Pharmacology and Chemotherapy
Academy of Medical Sciences of the USSR

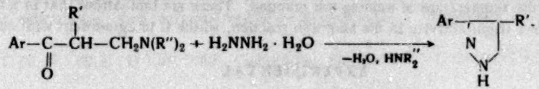
REACTIONS OF HYDRAZINE DERIVATIVES

XII. REACTION OF β-DIALKYLAMINO KETONES WITH HYDRAZINE

V. V. Ershov, A. N. Kost and A. P. Terentyev

In a previous communication [1] we had described the preparation of 3-arylpyrazolines by reacting the hydrochlorides of β-diethylaminopropiophenones with hydrazine hydrate in the presence of alkali. With this method we obtained 3-phenyl- (I), 3-p-tolyl- (II), 3-p-isopropylphenyl- (III), and 3-p-methoxyphenylpyrazoline (IV).

In the present study we extended the reaction to the aliphatic aromatic ketones for the purpose of studying its rules and to obtain pyrazolines that are difficultly accessible by other methods. It was revealed that the β-aminopropiophenones, having different substituents in both the ring and at the α-carbon atom of the side chain, readily enter into this reaction. In the latter case reaction with hydrazine leads to the formation of 3-aryl-4-alkylpyrazolines.



The reaction is not noticeably influenced by the presence of alkyl and alkoxyl groups in the nucleus. The yields remain high (Table, compounds II-VI) and only in the presence of branching are they reduced somewhat; thus, 3-p-isopropylphenylpyrazoline (III) was obtained in 75% yield and 3-(2,5-dimethylphenyl) pyrazoline (VII) in 64% yield. On the other hand, the presence of a nitro group in the ring sharply lowers the yield of the pyrazoline (VIII) to 56.9%. The 3-aryl-4-alkylpyrazolines (IX-XII) are obtained in lower yields than the 3-arylpyrazolines, i.e., the presence of a side chain somewhat hinders the reaction course. The yield of the pyrazoline decreases with increase in the length of the side chain. Thus, it dropped from 87% in the case of 3-phenyl-4-methylpyrazoline (IX) to 68% in the case of 3-phenyl-4-butylpyrazoline (XII).

In the principle the 5-substituted derivatives can also be obtained with the given method, but with greater difficulty than the gem-(4,4-or 5,5-) disubstituted pyrazolines, since replacement of the amino group in β-amino ketones proceeds more easily with the intermediate formation of a double bond [2]. This has been shown by Synder and co-workers [3] on the example of reacting phenylhydrazine with β-dimethylamino-α, α-dimethylpropiophenone.

All of the obtained 3-arylpyrazolines begin to decompose after several minutes in the air; however, they keep well for a long time under water. The introduction of substituents in the 4 position substantially increases the stability toward the action of atmospheric oxygen. For example, the 4-ethyl and 4-butylpyrazolines can be kept in the air for a day and longer.

Compound No.	Ar	R'	Yield Pyrazoline (in %)
(I)	C_6H_5	H	89
(II)	$p\text{-}CH_3C_6H_4$	H	93
(III)	$p\text{-}(CH_3)_2CHC_6H_4$	H	75
(IV)	$p\text{-}CH_3OC_6H_4$	H	86
(V)	$p\text{-}C_2H_5OC_6H_4$	H	88
(VI)	$p\text{-}C_2H_5C_6H_4$	H	80
(VII)	$p\text{-}2,5\text{-}(CH_3)_2C_6H_3$	H	64
(VIII)	$m\text{-}NO_2C_6H_4$	H	56.9
(IX)	C_6H_5	CH_3	87
(X)	C_6H_5	C_2H_5	73.2
(XI)	$p\text{-}CH_3C_6H_4$	C_2H_5	63
(XII)	C_6H_5	C_4H_9	68

The obtained pyrazolines were characterized as the solid 1-nitro derivatives. The bacteriological tests * revealed that 1-nitroso-3-p-tolylpyrazoline in vitro inhibits the growth of the human tubercle bacillus only at a concentration of 1:2000. The compound operates in a similar manner on Microsporum (1:8000), Trichophyton (1:4000) and Achorion (1:8000). This compound is not effective on actinomycetes, yeastlike fungi, acid-resistant saprophytes (in a concentration of 1:1000), and also on abdominal typhus and dysentery bacteria and coccus bacilli (in a concentration of 1:2000). 1-Nitroso-3-p-methoxyphenylpyrazoline is even less active. It is ineffective on the tubercle bacillus (1:1000) and shows only slight activity against the fungi: Microsporum (1:1000), Trichophyton (1:2000) and Achorion (1:2000).

We obtained the starting β-amino ketones by the Mannich reaction from the corresponding ketones. The data in the literature are extremely contradictory as to the optimum conditions for running this reaction, as well as to the use of various secondary amines. It can be seen that each series of ketones requires its own special set of conditions. It was found that the acetophenones, containing different substituents in the ring, are easily condensed with diethylamine hydrochloride and paraform when they are boiled in ethyl alcohol. However, the butyrophenones under these conditions form the β-diethylamino ketones in low yield [4]. We were also unable to obtain high yields when the reaction was run in dioxane and in butyl alcohol. Dimethylamine hydrochloride in dioxane medium gives with the butyrophenones and paraform the corresponding β-amino ketones in 70-75% yields; however, when the reaction is run in ethyl alcohol the yield of the α-dimethylaminomethylbutyrophenones drops to 40%. In this case the formation of the β-amino ketones strongly depends on the temperature of running the reaction. There are indications that in a number of cases [5] diethylamine shows slight activity in the Mannich reaction, which is in agreement with our observations.

EXPERIMENTAL

Preparation of Ketones. The method of Mowry and co-workers [6] was used to prepare the ketones by the Friedel-Crafts reaction, which involved running the reaction in carbon tetrachloride medium in the presence of aluminum chloride at 0-5°. It was found that under these conditions the ketones are obtained in good yields not only with acetyl chloride, but also with the chlorides of propionic, butyric and caproic acids. With this method we obtained: p-methylacetophenone, b. p. 110° (12 mm). yield 93%; p-ethylacetophenone, b. p. 113-114° (12 mm), yield 91%; p-isopropylacetophenone, b. p. 120-121° (10 mm), yield 90%; 2,5-dimethylacetophenone, b. p. 80° (3 mm), yield 80%; p-methoxyacetophenone, m. p. 38-39°, yield 84%; p-ethoxyacetophenone, b. p. 136° (10 mm), yield 73%; propiophenone, b. p. 85° (7 mm), yield 77%; butyrophenone, b. p. 74° (3 mm), yield 80%; p- methylbutyrophenone, b. p. 88-89° (3 mm), yield 78%; 2,5-dimethylbutyrophenone, b. p. 98-99° (4 mm), yield 86%; and caprophenone, b. p. 124-125° (9 mm), yield 80%. Hydrocinnamoyl chloride under these conditions gives indanone in 81% yield. m-Nitroacetophenone was obtained by the nitration of acetophenone.

Mannich Bases. a) A mixture of 0.5 mole of ketone, 0.5 mole of diethylamine hydrochloride, 18 g of finely-ground paraform and 40 ml of ethyl alcohol was boiled for 4-6 hours. If the solution failed to become clear, then 1 ml of concentrated hydrochloric acid was added and the boiling continued another 2-3 hours. The mixture was diluted with 3 volumes of water, washed with ether, made alkaline, and the free amino ketone extracted with ether, which was isolated as the salt by passing hydrogen chloride through the dry ether solution, and then vacuum-dried. The yield of β-diethylamino-p-ethoxypropiophenone

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* The testing was done by S. N. Milovanova in the S. Ordzhonikidze All-Union Scientific-Research Chemical-Pharmaceutical Institute.

hydrochloride was 66 %, m. p. 135-136°; of β-diethylamino-p-ethylpropiophenone hydrochloride 66 %, m. p. 122°; and of β-diethylamino-2,5-dimethylpropiophenone hydrochloride 60 %, m. p. 110-112°.

b) A mixture of 0.2 mole of ketone, 0.25 mole of dimethylamine hydrochloride, 7 g of paraform and 20 ml of dioxane was boiled for 5 hours. The amino ketone was isolated in the same manner as described above, distilling off the excess dimethylamine with part of the ether. The yield of α-dimethylaminomethylpropiophenone hydrochloride was 67 %, m. p. 155-157° (literature: m. p. 153-154° [4]); of α-dimethylaminomethylbutyrophenone hydrochloride 75%, m. p. 142° (literature: m. p. 142.5° [7]); of α-dimethylaminomethyl-p-methylbutyrophenone hydrochloride 77.6 %, m. p. 179°; and of α-dimethylaminomethylcaprophenone hydrochloride 72 %, m. p. 129°.

β-Diethylamino-m-nitroproprlophenone was obtained by the earlier described [8] method, m. p. 124°. Literature: m. p. 122° [8].

3-p-Ethoxyphenylpyrazoline (V). To a mixture of 20 ml of hydrazine hydrate, 10 ml of 40 % sodium hydroxide solution and 25 ml of methyl alcohol with heating and vigorous stirring was added dropwise in one hour a solution of 27 g of β-diethylamino-p-ethoxypropriophenone hydrochloride in 50 ml of methyl alcohol, and the mixture was boiled another hour. After distilling off the methyl alcohol in vacuo (in a nitrogen stream) the 3-p-ethoxyphenylpyrazoline deposited as a crystalline mass, which was washed with water to remove any free hydrazine. Yield 88 %, m. p. 82-85°.

To obtain the N-nitroso derivative a solution of 17 g of pyrazoline (V) in 2N hydrochloric acid was treated with cooling with a concentrated solution of sodium nitrite. The obtained 1-nitroso-3-p-ethoxyphenylpyrazoline was recrystallized from methyl alcohol. Yield 19 g (96%), m. p. 142-143°.

Found %: C 60.38, 60.37; H 6.19, 6.14. $C_{11}H_{13}O_2N_3$. Calculated %: C 60.35; H 5.97.

1-Butyryl-3-p-ethoxyphenylpyrazoline was made by the addition of butyryl chloride to a benzene solution of 3-p-ethoxyphenylpyrazoline (V) in the presence of 2N alkali solution with subsequent heating for 30 minutes. The dry benzene solution was evaporated, the residue dissolved in acetone, and water added to precipitate crystals, which were then recrystallized twice from acetone. Yield 54%, m. p. 106.5-107°.

Found %: C 69.12, 69.15; H 7.85, 7.89. $C_{15}H_{20}O_2N_2$. Calculated %: C 69.20; H 7.75.

3-p-Ethylphenylpyrazoline (VI). Obtained by the method described for pyrazoline (V). Yield 80%, m. p. 47-49°. N-Nitroso derivative, m. p. 106°.

Found %: C 65.22, 65.25; H 6.62, 6.60. $C_{11}H_{13}ON_3$. Calculated % C 65.00; H 6.46.

1-Acetyl-3-p-ethylphenylpyrazoline, m. p. 81° (from ether).

Found %: C 71.91, 71.95; H 7.30, 7.30. $C_{13}H_{16}ON_2$. Calculated %: C 72.18; H 7.46.

3-(2,5-Dimethylphenyl)pyrazoline (VII). Obtained in the same manner, but isolated after distilling off the solvent as a thick oil with b. p. 137° (3 mm), n^{20}_D 1.5943, yield 64.1%. N-Nitroso derivative, m. p. 112°.

Found %: C 64.95, 64.89; H 6.74, 6.79. $C_{11}H_{13}ON_3$. Calculated %: C 65.00; H 6.46.

3-m-Nitrophenylpyrazoline (VIII). Obtained in the same manner as (V). Yield 56.9%, m. p. 112-115°. N-Nitroso derivative, m. p. 139°.

Found %: C 49.34, 49.39; H 3.84, 3.90. $C_9H_8O_3N_4$. Calculated %: C 49.09; H 3.66.

3-Phenyl-4-methylpyrazoline (IX). Obtained in the same manner. Yield 87%; m. p. 109-111°. N-Nitroso derivative, m. p. 90° (from aqueous alcohol).

Found %: C 63.59, 63.70, H 6.08, 6.10. $C_{10}H_{11}ON_3$. Calculated %: C 63.50, H 5.86.

3-Phenyl-ethylpyrazoline (X). Obtained in the same manner as (V), but after distilling off the solvent the residue was extracted with ether. The ether solution was dried over potash, the ether distilled off, and the residue vacuum-distilled (in a nitrogen stream). Yield 73.2%, b. p. 127-129° (5 mm), m. p. 40-42°, n^{20}_D 1.5895. N-Nitroso derivative, m. p. 81° (from petroleum ether or aqueous alcohol).

Found %: C 65.23, 65.25; H 6.64, 6.67. $C_{11}H_{13}ON_3$. Calculated %: C 65.00; H 6.46.

N-Phenylcarbamido derivative, m. p. 123° (from alcohol).

Found %: N 14.40, 14.47. $C_{18}H_{19}ON_3$. Calculated %: N 14.33.

3-p-Tolyl-4-ethylpyrazoline (XI). Obtained in the same manner as (X). Yield 63%, b. p. 140 – 141° (5 mm), n^{20}_D 1.5290, d^{20}_4 0.9748, MR_D 59.56; calc. 57.68% [*]; EM_D 1.88. According to the data of Auwers [10], EM_D for various 3-phenylpyrazolines varies from +1.7 to +1.9.

The N-benzoyl derivative was obtained by benzoylation with benzoic anhydride in benzene solution. M. p. 103° (from petroleum ether).

Found %: C 77.75, 77.79; H 7.03, 7.08. $C_{19}H_{20}ON_2$. Calculated %: C 78.03; H 6.89.

3-Phenyl-4-butylpyrazoline (XII). Obtained in the same manner as (X). Yield 68%, b. p. 150 – 151° (5 mm), m. p. 36–38°, n^{20}_D 1.5689. N-Nitroso derivative, m. p. 68° (from alcohol).

Found %: C 67.59, 67.63; H 7.58, 7.62. $C_{13}H_{17}ON_3$. Calculated %: C 67.50; H 7.41.

SUMMARY

1. The aminomethylation of a number of alkyl aryl ketones gave the corresponding β-dialkylamino ketones, which when reacted with hydrazine hydrate were converted into 3-arylpyrazolines in good yields.

2. The possibility of using this method to synthesize 3-aryl-4-alkylpyrazolines was shown.

LITERATURE CITED

[1] A. N. Kost and V. V. Ershov, Bull. Moscow State University, No. 12, p. 115 (1955).

[2] H. Hellman, Z. angew. Ch., 65, 473 (1953); H. Snyder, J. Brewster, J. Am. Chem. Soc., 70, 4230 (1948).

[3] H. Snyder, J. Brewster, J. Am. Chem. Soc., 71, 1061 (1949).

[4] A. Ruddy, J. Buckley, J. Am. Chem. Soc., 72, 718 (1950).

[5] W. Kermack. W. Muir, J. Chem. Soc., 1931, 3089; G. A. Levy and H. B. Nisbet, J. Chem. Soc., 1938, 1053.

[6] D. Mowry, M. Renoll, W. Huber, J. Am. Chem. Soc. 68, 1105 (1946).

[7] E. Knott, J. Chem. Soc., 1947, 1190.

[8] C. Mannich, M. Dannehl, Arch. Pharm., 276, 206 (1938).

[9] A. N. Kost and I. I. Grandberg, J. Gen. Chem., 26, 1717 (1956).[**]

[10] K. Auwers, P. Heimke, Lieb. Ann., 458, 175 (1927).

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[*] The refraction for =N-N- was taken equal to 5.871 [9].

[**] Original Russian pagination. See C.B. Translation.

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Moscow State University

SYNTHESES WITH ACRYLONITRILE

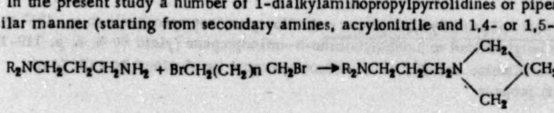
XXX. SOME 1-SUBSTITUTED PYRROLIDINES AND PIPERIDINES

A. P. Terentyev and A. N. Kost

By reacting dialkylaminoalkylamines with succinic anhydride and subsequent reduction with lithium aluminum hydride, Rice, Grogan and Reid [1] synthesized a number of 1-dialkylaminoalkylpyrrolidines, the methiodides of which show hypotensive action.

Earlier one of us [2] had described the synthesis of 1,3-di(N-piperidyl)-propane, based on the cyanoethylation of piperidine with subsequent reduction of the obtained aminonitrile and further reaction of the formed diamine with 1,5-dibromopentane.

In the present study a number of 1-dialkylaminopropylpyrrolidines or piperidines were synthesized in a similar manner (starting from secondary amines, acrylonitrile and 1,4- or 1,5-dibromides):



$$R_2NCH_2CH_2CH_2NH_2 + BrCH_2(CH_2)_nCH_2Br \rightarrow R_2NCH_2CH_2CH_2N\begin{matrix} CH_2 \\ \\ CH_2 \end{matrix}(CH_2)_n.$$

n = 2, 3.

The cyanoethylation of 2,4-dimethylpyrrole gave β-(2,4-dimethyl-1-pyrrolyl) propionitrile, from which by reduction over skeletal nickel we were unable to isolate the corresponding diamine (propylamine and 2,4-dimethylpyrrolidine were obtained in small yield).

EXPERIMENTAL

1,4-Dibromobutane was obtained by the treatment of 1,4-butanediol with bromine and red phosphorus. Yield 89%, b. p. 79 – 80° (7 mm); n_D^{20} 1.5199. 1,5-Dibromopentane was obtained in the usual manner from benzoylpiperidine. B. p. 111 – 112° (20 mm), n_D^{20} 1.5178. The careful addition of 0.2 mole of freshly distilled methyl iodide to a solution of 0.1 mole of 1,3-di(N-piperidyl) propane [2] in 50 ml of dry ether with subsequent heating for 20-30 minutes under reflux gave the dimethiodide of 1,3-di(N-piperidyl) propane, m. p. 300°(from alcohol).

Found %: N 5.59, 5.64. $C_{15}H_{32}N_{22}I_2$. Calculated %: N 5.67.

1-(N-Pyrrolidyl)-3-(N-piperidyl)propane. A mixture of 9.5 g of 1-(γ-aminopropyl) piperidine [2, 3], 18 g of 1,4-dibromobutane, 35 ml of benzene and 11 g of potash, moistened with several drops of water, was boiled with stirring for 8 hours. Then 20 ml of a 40% aqueous sodium hydroxide solution was added and the amine and benzene were steam-distilled into hydrochloric acid. The benzene was separated from the distillate, washed twice with 5% hydrochloric acid, the water layer and acid extracts evaporated, the residue decomposed with alkali, extracted with ether, and after drying over fused potassium hydroxide, distilled. The yield of 1-(N-pyrrolidyl)-3-(N-piperidyl) propane was 9.6 g (70%).

B. p. 131.5–132° (11 mm); n_D^{20} 1.4830, d_4^{20} 0.9183, MR_D 60.96; calc. 61.09.

Found %: C 73.40, 73.49; H 12.29, 12.40. $C_{12}H_{24}N_2$. Calculated %: C 73.53; H 12.34.

The dipicrate was obtained by mixing ether solutions of the diamine and picric acid. After recrystallization from alcohol, m. p. 176.5°.

Dimethiodide, m. p. 305° (from alcohol).

Found %: N 5.89, 5.96. $C_{14}H_{30}N_2I_2$. Calculated %: N 5.83.

1-Diethylamino-3-(N-pyrrolidyl)propane. Obtained in a similar manner from 9.2 g of 1-diethylamino-3-aminopropane [4] and 18 g of 1,4-dibromobutane. Yield 6.0 g (48%), b. p. 74° (3 mm); n_D^{20} 1.4577; d_4^{20} 0.8530, MR_D 58.88; calc. 58.74.

Dipicrate, m. p. 165.5° (from alcohol).

Found %: N 17.36, 17.41. $C_{11}H_{24}N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: N 17.44.

Dimethiodide, m. p. 272.5° (decompn., from alcohol).

1-Diethylamino-3-(N-piperidyl) propane. Obtained from the same diamine, but with 1,5-dibromopentane. Yield 62%, b. p. 124° (17 mm), n_D^{20} 1.4740.

Dipicrate, m. p. 150° (from alcohol).

Found %: C 43.81, 43.88; H 4.83, 4.99. $C_{12}H_{26}N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: C 43.90; H 4.91.

1-Dibutylamino-3-(N-piperidyl)propane. β-Dibutylaminopropionitrile (b. p. 135° at 20 mm [5]) was reduced with sodium in butyl alcohol to 1-dibutylamino-3-aminopropane (yield 60 %, b. p. 119-120° at 19 mm [6]). From 19 g of this diamine and 23 g of 1,5-dibromopentane we obtained 14 g (56%) of 1-dibutylamino-3-(N-piperidyl) propane.

B. p. 140° (1 mm), 167–168° (14 mm), n_D^{20} 1.4610, d_4^{20} 0.8551, MR_D 81.65; calc. 81.75.

Found %: N 11.06, 11.15. $C_{16}H_{34}N_2$. Calculated %: N 11.01.

Dipicrate, m. p. 171-172° (from alcohol).

2,4-Dimethyl-1-(2'-cyanoethyl) pyrrole. To a solution of 13 g of 2,4-dimethylpyrrole b. p. 163–164° and 751 mm, n_D^{20} 1.4890) in 50 ml of dioxane was added 0.2 ml of Rodionov catalyst (an alcohol solution of trimethylphenylammonium ethoxide) and then with vigorous stirring was added 10 ml of acrylonitrile in 0.5 hour. The temperature of the mixture was maintained at about 40°, at first by heating, and then by cooling with water. After adding the acrylonitrile the reaction mass was stirred (at 40°) another 4 hours, then it was cooled to room temperature and poured into 200 ml of water. Then the mass was acidified (to Congo) with acetic acid, the floating oil extracted with either, the ether extract dried over potash, the ether distilled off, and the residue vacuum-distilled. At first the unreacted 2,4-dimethylpyrrole distilled (b. p. 90-94° at 55 mm), and then 12 g (58%) of 2,4-dimethyl-1-(2'cyanoethyl) pyrrole.

B. p. 152 – 153° (18 mm), n_D^{25} 1.5048; d_4^{25} 0.9878, MR_D 44.48; calc. 44.29.

Found %: N 19.08, 19.19. $C_9H_{12}N_2$. Calculated %: N 18.90.

SUMMARY

The reduction of β-dialkylaminopropionitriles gave the corresponding diamines, which with tetra-or pentamethylene dibromide were converted into the corresponding 1-substituted pyrrolidines or piperidines.

LITERATURE CITED

[1] L. Rice, C. Grogan, E. Reid, J. Am. Chem. Soc., 75, 2261 (1953); see also S Friess, W. McCarville, J. Am. Chem. Soc. 76, 1367 (1954).

[2] A. P. Terentyev and E. A. Terentyeva, J. Gen. Chem., 12, 415 (1942).

[3] A. P. Terentyev and A. N. Kost, J. Gen. Chem., 18, 510 (1948).

[4] A. P. Terentyev and A. N. Kost J. Gen. Chem., 16, 859 (1946).

[5] A. P. Terentyev, A. N. Kost and S. M. Gurvich, J. Gen. Chem., 22, 1977 (1952) (T. p. 2027).*

[6] F. Whitmore, H. Mosher, R. Adams, R. Taylor, E. Chapin, C. Weisel, W. Yanko, J. Am. Chem. Soc., 66, 725 (1944).

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---

* T. p. = C. B. Translation pagination.

[1] L. Hine, C. Grogan, E. [illegible] J. [illegible] Chem. Soc., [illegible] (195[illegible]); [illegible]
J. Am. Chem. Soc. 76, 1884 (1954).

[2] A. A. Tenetnyov and I. A. Tecntnyova, Gen. [illegible] (1949).

[3] A. E. [illegible] and A. N. [illegible]

[4] [illegible]

[5] A. A. Terentyev, A. N. [illegible]

[6] F. Whitmore, H. [illegible], R. [illegible], E. Taylor, [illegible] Soc., 66, 728 (1944).

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PREPARATION OF TETRAETHYLAMMONIUM BASES FOR POLAROGRAPHIC PURPOSES ON AN ANIONITE

M. N. Platonova

In a number of cases for the polarographing of organic compounds it is necessary to use ground electrolytes, the reduction potentials of which lie in a region more negative than - 1.8 v. The quaternary ammonium compounds: tetramethyl-, tetraethyl- and tetrabutylammonium halides and their corresponding bases, show such a reduction potential. In organic chemistry these salts are synthesized from tertiary amines and alkyl halides.

For exact polarographic measurements, and specifically: to determine $E_{1/2}$, the number of electrons, participating in the electrochemical reaction, and the diffusion coefficient, it is preferable to operate in solutions that possess buffer properties, and for this, together with the salts, it is necessary to make use of the bases of quaternary ammonium compounds. These bases are usually obtained from the salts by treating them with moist Ag_2O, i.e. a method that requires a large consumption of silver nitrate.

In the present study to obtain bases suitable for polarographic purposes we employed the process of converting tetraethylammonium chloride on an anionite.

For this it was necessary to: 1) determine the conditions under which the tetraethylammonium base could be obtained when using an anionite, and 2) study the suitability of the obtained base for the preparation of a polarographic ground.

A large number of papers have been published in the literature on the subject of the exchange of inorganic compounds on anionites [1, 2], but comparatively little data exists on the behavior of anionites toward salts containing organic radicals.

It was established that anionites liberate hydroxyl ions in solution, exchanging them for Cl' or SO_4'', in which connection the exchange capacity of anionites with respect to the hydroxyl ion depends to a considerable degree on their basicity. The weakly basic anionites, not dissociating in a medium with a high pH, show slight exchange of the OH', whereas the strongly basic anionites do not lower their activity even in alkaline solutions [3].

For our studies we used 2 specimens of Anionites AN-2F and EDE-10. Preliminary experiments revealed that Anionite AN-2F is not suitable for these purposes, and consequently the further work was done with Anionite EDÈ-10, showing strongly basic properties.

EXPERIMENTAL

In our work the column containing the anionite had a height of 300-500 mm and a diameter of 14 mm. The studies were run at 18°. The anionite was saturated with OH' ions by treatment with either 0.75-1.00M KOH or NaOH solution. After this the column was thoroughly eluted from excess regenerating solution to negative reaction for alkali. The wash waters after the anionite were polarographically tested for the absence of alkali metal ions.

A Gorkovsky Model M-7 polarograph and a M-21 galvanometer with a scale sensitivity of $0.91 \cdot 10^{-9}$ amp/mm was employed to polarograph the solutions at a distance of 1.5 m. The cylindrical, not constricted capillary had the following characteristics: $t = 3.5$ sec., $L = m^{2/3} t^{1/6} = 1.99$ mg$^{2/3}$·sec.$^{-1/2}$ at zero potential, and length 11.25 cm.

In the study we used tetraethylammonium chloride solutions ranging in concentration from 0.75-0.15N, which due to hydrolysis showed a weakly acid reaction. More highly concentrated solutions were not studied, since here insufficient exchange on anionites is observed. For polarographic purposes grounds are usually used, containing quaternary ammonium compounds in the concentration limits of 0.3-0.01N.

The experiments were run under the following conditions: The height of the anionite layer was 300 mm and the filtration rate was about 1 ml/cm^2 · min.; 100 ml of solution was passed through the column and 10 ml samples were taken after the anionite. The alkalinity and chlorine content in each fraction were determined by titration.

The experimental results are shown in Fig. 1-3, where the yield curves after the anionite are given. In all of the Figures Curve 1 refers to the sum of OH' and Cl' after the anionite, expressed in equivalents; Curve 2 shows the change in Cl' concentration; and Curve 3 shows the change in the OH' concentration after the anionite layer.

The more concentrated the solution, the more rapid is the passage of the chloride ion and the sharper is the maximum on the yield curve, showing the change in the hydroxyl ion concentration after the anionite. The most complete exchange under the given conditions is observed at a tetraethylammonium concentration of 0.15N (Fig. 3). In this case the salt is almost completely converted (100-90%) into the base.

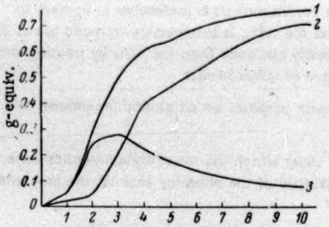


Fig. 1. Yield curve after the anionite (concentration of $(C_2H_5)_4NCl$ 0.75 N, height of layer 300 mm). 1) total content of Cl' and OH', 2) Cl' content 3) OH' content, 4) g-equiv. 4) Number of the filtrate fraction.

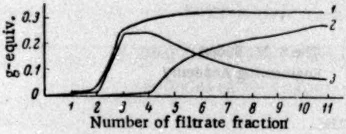
Higher concentration of the base can be obtained by careful evaporation of this solution or by taking the first fractions of the filtrate when the more concentrated solutions (0.33N, see Fig. 2) are passed through the anionite. When this is done it is possible to convert the salt to the base in the first portions of the filtrate to the extent of 80-70%. When the solution concentration is 0.75N the conversion to the base in the individual fractions is at best only 40%.

To enhance the exchange effect we ran some experiments with a higher anionite layer. The yield curve for the experiment, run in the same column, but with a layer height of 530 mm and a salt solution concentration of 0.33N, is shown in Fig. 4. On this curve an increase in the passage rate of the chloride ion proceeds more slowly, and the yield percent in the individual fractions rises to 87% (compare with the curve in Fig. 2, where at a concentration of 0.33N and an anionite layer height of 300 mm the yield is equal to 80%.)

From this experiment it can be seen that an increase in the length of the layer naturally increases the yield of base after the column; however, a column with a greater height of the layer is washed free of the regenerating solution, i.e., of KOH or NaOH, with extreme difficulty. The absence of alkali metal ions is especially important for polarographic purposes, since these impurities can give waves in the range of potentials ranging from -1.8 to -2.4 v. Consequently, in some cases it is preferable to collect more dilute solutions after the column, but free of alkali metal ion impurities.

The last portions of the filtrate, in which the passage of the salt is already substantial, can be passed a second time through the anionite or they can be used directly for the preparation of buffer mixtures.

The polarogram of one of the filtrates after the anionite (at a 0.02M concentration in a mixture containing 50% ethyl alcohol) is shown in Fig. 5 (Curve 1), from which it can be seen that with the given measurement sensitivity a noticeable contamination by the ions of alkali metals is not observed.



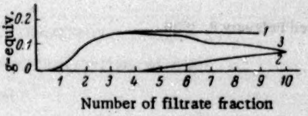
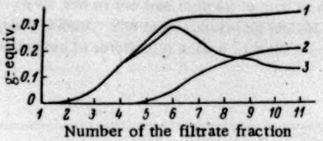


Fig. 2. Yield curve after the anionite (concentration of $(C_2H_5)_4NCl$ 0.33 N, height of layer 300 mm).

Fig. 3. Yield curve after the anionite (concentration of $(C_2H_5)_4NCl$ 0.15 N, height of layer 300 mm).



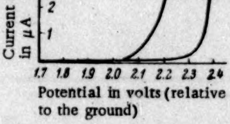


Fig. 4. 1 Yield curve after the anionite (concentration of $(C_2H_5)_4$ NCl 0.33N, height of layer 530 mm).

Fig. 5. Polarogram of the solution after the anionite.

Curve 2 in Fig. 5 gives the wave for potassium, introduced into this solution after the anionite as KCl (concentration 0.0005M).

In the present study we used a column with a diameter of 14 mm; in case of need its dimensions can be increased for treating larger volumes of liquids.

SUMMARY

1. It was established that dilute solutions of the tetraethylammonium base can be obtained from its chloride on Anionite EDE-10.

2. The most complete conversion to the base is achieved at a salt concentration in the solution of 0.15 N.

3. Substantial contamination by alkali metal ions is not observed here, and the solutions of the base are suitable for polarographic purposes at potentials more negative than -1.8 v.

LITERATURE CITED

[1] C. W. Davies, G. H. Nancollas, Nature, 165, 237 (1950).

[2] L. S. Aleksandrova, T. B. Gapon, et al, Trans. Commission on Analytical Chemistry, Vol. VI (IX), p. 235 (1955).

[3] O. Samuelson, Utilization of Ionic Exchange in Analytical Chemistry, Moscow, p. 29 (1955).

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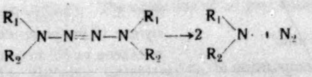
The S. M. Buden
Engineering Academy

FREE RADICAL REACTIONS IN SOLUTIONS

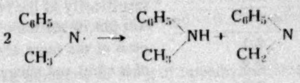
IX. DIMETHYLDIPHENYLTETRAZENE AND TETRAMETHYLTETRAZENE AS SOURCES OF FREE RADICALS WITH A REACTION CENTER ON THE NITROGEN ATOM

B. L. Erusalimsky, B. A. Dolgoplosk and A. P. Kavunenko

In numerous investigations, devoted to a study of free radical reactions in a condensed phase, comparatively little attention has been given to free radicals with a reaction center on the nitrogen, sulfur or oxygen atoms, the behavior of which in many chemical reactions can strongly differ from the alkyl and aryl free radicals. Of such " heteroradicals " the radicals of the type RO · have been studied most completely, while the radicals RS · and RṄR have been studied to a lesser degree. In the present study we give the first data obtained by us in studying the free radicals with a reaction center on the nitrogen atom. The information given in the literature relative to free radicals of the RNR type is associated for the most part with a study of the aryl-substituted hydrazines, which from the time of Wieland's studies became the subject of numerous investigations. The basic purpose of the indicated studies was to determine the stability of hydrazine derivatives and of the free radicals formed in their dissociation as a function of the nature of the substituents on the N-atoms. The most convenient sources of this type of free radicals are the tetrazenes, which decompose when heated in solution in accord with the equation:



In the studies of Wieland [1] and of some other authors [2, 3], devoted to a study of the decomposition products of tetrazenes in various media, it is concluded that the free radicals formed during the reaction course show disproportionation, for example:



The question as to the possibility of the free radicals reacting with the solvent or of their being involved in other reactions is not discussed in the indicated studies and in later investigations [4]. The results obtained in the present study show that radicals of the RṄR type are extremely active in the reactions for the cleavage of the H atom from hydrocarbon molecules, addition to a vinyl double bond, and those capable of initiating polymerization. On the example of dimethyldiphenyltetrazene we established the monomolecular nature of the decomposition shown by tetrazenes when heated in solution, which ensues from the fact that the reaction rate constant is independent of the tetrazene concentration (Table and Fig. 1).

The energy of activation for this reaction, calculated from the kinetics data using the Arrhenius equation, is 33 kcal./mole. Thermally, tetramethyltetrazene is much more stable. At 130° this compound shows very slow decomposition in solution. The rate constant for the decomposition of tetramethyltetrazene in isopropylbenzene solution at 145° and a concentration of 0.7 mole% is $0.56 \cdot 10^{-4}$ sec. $^{-1}$.

The ability of free radicals with a reaction center on the nitrogen atom to initiate polymerization was shown on the example of the system styrene-dimethyldiphenyltetrazene (Fig. 2).

We established the ability of alkylnitrogen radicals to react with saturated and unsaturated hydrocarbons on the basis of studying the thermal decomposition products of tetramethyltetrazene in isopropylbenzene and in α-methylstyrene. The main reaction products in the first case are dimethylamine (92.3 % yield) and dicumenyl, i. e., 2,3-dimethyl-2,3-diphenylbutane (43.9% yield). The high yield of dimethylamine and the formation of dicumenyl, being the result of two consecutive reactions (3) and (4), indicate that the basic source for the formation of dimethylamine must be considered to be not the disproportionation of the free dimethylnitrogen radicals (Reaction (2)), but the cleavage of an H atom by these radicals from isopropylbenzene:

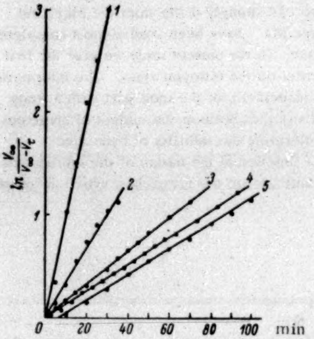


Fig. 1. Kinetics for the thermal decomposition of dimethyldiphenyltetrazene in isopropylbenzene solution.

1 — 140°, concn. 0.57 mole %; 2— 130°, concn. 0.69 mole %; 3 — 120°, concn. 18.00 mole %; 4 — 120°, concn. 0.65 mole %; 5 — 120°, concn. 6.07 mole %.

TABLE

Rate Constants For Thermal Decomposition Reaction of Dimethyldiphenyltetrazene in Isopropylbenzene Solution

Exptl. temp.	Tetrazene conc. (mole %)	$K \cdot 10^4$ sec.$^{-1}$
120°	0.65	2.1
120	6.07	2.2
120	18.00	2.7
130	0.69	6.5
140	0.57	16.7

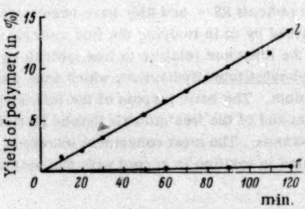


Fig. 2. Kinetics for the polymerization of styrene in the presence of dimethyldiphenyltetrazene at 85° in a nitrogen atmosphere.

1 — without the tetrazene, 2 — 0.324 mole % of the tetrazene. 3 Yield of polymer (in %).

Proceeding from the fact that the disproportionation reaction is associated with the formation of equivalent amounts of saturated and unsaturated components, it can be concluded that as an extreme 84.6% of the dimethylamine (of the theoretical) was formed specifically as the result of Reaction (3). • This fact places the dimethylnitrogen radical in the class of the more active free radicals of the type of methyl and phenyl, showing their greatest reaction capacity in the acts of rupturing an H atom from hydrocarbons. The absence of a

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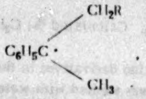
• This conclusion follows from the assumption that the fraction of the alkylnitrogen radicals that did not show up as dimethylamine (i. e., 7.7% of the theoretical), participated in the disproportionation reaction and led to the formation of the unsaturated component. If such a postulation is valid, then this amount of dimethylamine (7.7%) was formed by Reaction (2).

sufficiently complete agreement between the yields of dimethylamine and dicumenyl is apparently associated with the fact that the cumenyl free radicals, formed by Reaction (3), participate together with the recombination and acts (4) in the disproportionation reaction, either with each other or with the dimethylnitrogen free radicals. That such reactions are probable is indicated by the presence of unsaturated compounds, established in the reaction mixture, formed as the result of tetramethyltetrazene decomposition in isopropylbenzene. The disproportionation reaction is the predominant reaction for certain radicals of the



type, in their structure close to that of the cumenyl free radical, which was shown in studying the reaction products of α-methylstyrene with the free radical $(CH_3)_2CCN$.*

When the thermal decomposition of tetramethyltetrazene was run in α-methylstyrene medium we established that absolutely no dimethylamine is formed under these conditions. The dimethylnitrogen free radicals arising in the decomposition of the tetrazene react quantitatively with the vinyl double bonds of α-methylstyrene. As a result, in this case also the dimethylnitrogen radicals show a behavior that is completely analogous to the methyl free radicals, which under similar conditions are quantitatively ensnared by α-methylstyrene. The complete absence of dimethylamine in the decomposition products of tetramethyltetrazene in α-methylstyrene indicates that in the given case the free dimethylnitrogen radicals completely fail to show disproportionation.

EXPERIMENTAL

Synthesis of Tetrazenes. The tetrazenes were synthesized using the method described by Fischer [2], namely by the oxidation of the corresponding disubstituted unsymmetrical hydrazines with yellow mercuric oxide.

a) **Dimethyldiphenyltetrazene.** The starting methylphenylhydrazine was obtained by the reduction of nitrosomethylaniline with zinc dust in acetic acid. The oxidation of 11 g of the methylphenylhydrazine gave 5 g of the tetrazene (45.4% yield), m. p. 138° (in the literature 137° [2]).

Found %: C 69.88, 69.92; H 7.41, 7.31. $C_{14}H_{16}N_4$. Calculated %: C 70.0; H 6.67.

b) **Tetramethyltetrazene.** The oxidation of 50 g of dimethylhydrazine gave 25 g of the tetrazene (50% yield), b. p. 74° at 110 mm.

Found %: N 47.93, 48.14. $C_4H_{12}N_4$. Calculated %: N 48.30.

Decomposition Kinetics of Tetrazenes. The thermal decomposition rate of the tetrazenes was determined from the amount of nitrogen evolved during reaction. To absorb the dimethylamine, formed in the decomposition of tetramethyltetrazene, a trap containing acid was placed ahead of the gas burette.

Polymerization of Styrene. The polymerization experiments were run in a nitrogen atmosphere in ampuls with graduated necks. The rate of the polymerization process was calculated from the degree of contraction.

Study of the Tetramethyltetrazene Decomposition Products. The thermal decomposition of tetramethyltetrazene was run in accord with the method described earlier for the triazenes [5].

a) A solution of 8 g of the tetrazene in 130 g of isopropylbenzene (concentration of the tetrazene 6.5 mole %) was decomposed at 145°. The reaction was run until nitrogen evolution ceased (36 hours). Most of the dimethylamine was absorbed in two traps containing 3N sulfuric acid and connected in series. To effect more complete removal of the amine from the reaction mixture the latter, on conclusion of reaction, was blown with nitrogen for 5-6 hours at 110°. The amount of dimethylamine in the traps, based on the titration data, was 5.03 g (80.1% of the theoretical). The dimethylamine was characterized as the mercury derivative. To obtain the latter a sulfuric acid solution of the amine was made alkaline, and the evolved free amine was bubbled through a dilute solution of mercuric chloride in anhydrous ethyl alcohol [6]. After recrystallization from boiling ethyl alcohol the mercury derivative was analyzed by titration for the amount of amine.

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* The data on the reaction of the methyl and dimethylcyanomethyl free radicals with α-methylstyrene were obtained in our laboratory by E.B. Milovsky.

Found %: C_2H_7N. 14.15, 14.46. $C_2H_7NHgCl_2$. Calculated %: C_2H_7N. 14.24.

Based on the titration data, the amount of amino derivatives in the hydrocarbon phase corresponded to 17.6% of the theoretical. The reaction mixture was washed with water, and the water extract was established to contain 0.76 g of dimethylamine, which was characterized as the mercury derivative. The total yield of dimethylamine was 5.79 g (92.3%). The water-insoluble amino derivatives, present in the hydrocarbon phase in small amount, were removed by washing with dilute hydrochloric acid. From the acid solution we isolated 0.02 g of oily substance, having an amine character, which was not studied further. From the hydrocarbon layer after distilling off the solvent we isolated 7.36 g of 2,3-dimethyl-2,3diphenylbutane (dicumenyl). M. p. 118.5-119°.(in the literature 120° [7]). Yield 43.9%. In a separate sample of the reaction mixture, not subjected to the above treatment, we established by hydrogenation in alcohol solution over palladium the presence of unsaturated compounds. The amount taken for the hydrogenation was 1.9840 g. The amount of hydrogen absorbed was 13.1 ml (NTP).

b) A solution of 0.176 g of tetramethyltetrazene in 18.2 g of α-methylstyrene (concentration 0.8 mole %) was decomposed at 145°. The evolved gas was pure nitrogen. Dimethylamine was absent in both the gas and liquid phases. The reaction products present in the hydrocarbon phase were not investigated.

SUMMARY

1. The kinetics for the thermal decomposition of dimethyldiphenyltetrazene in isopropyl solution was studied, the energy of activation for this process was calculated, and it was shown that the decomposition of the tetrazene proceeds by a monomolecular mechanism.

2. The high activity of the dimethylnitrogen free radical was established: a) in the reaction for H-atom cleavage, and b) in the reaction for addition to a vinyl double bond.

LITERATURE CITED

[1] H. Wieland, Lieb. Ann., 392, 138, 144, 147 (1912).

[2] E. Fischer, Lieb. Ann., 190, 182 (1878); 199, 166, 319, 326, (1879).

[3] E. Renouf, Ber., 13, 2173 (1880).

[4] C. G. Overberger, B. S. Marks, J. Am. Chem. Soc., 77, 4097 (1955).

[5] B. A. Dolgoplosk, B. L. Erusalimsky, V. A. Krol and L. M. Romanov, J. Gen. Chem., 24, 1775 (1954). (T. p. 1745). •

[6] K. A. Hofmann, E. C. Marburg, Lieb. Ann., 305, 202 (1899).

[7] Beilst., V, 396.

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Institute of High-Molecular Compounds
Academy of Sciences of the USSR

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THE PREPARATION OF NITRATES OF TETRASUBSTITUTED PHOSPHONIUM AND ARSONIUM BASES

G. V. Medoks and E. M. Soshestvenskaya

The nitrates of tetrasubstituted phosphonium and arsonium bases can be used both in analytical chemistry [1] and to obtain binary salts with the nitrates of the rare earth elements [2], strongly differing, in a number of cases, in solubility and showing different melting points, and even being salts of the neighboring lanthanides.

Usually these nitrates are obtained by the neutralization of the free bases with nitric acid, obtained in turn by the direct reaction of the halides with a suspension of silver oxide in water, or as the end result of the exchange decomposition of the halides of the bases with silver nitrate, and in individual cases – with nitric acid [3-7].

Taking into consideration the poorer solubility of certain nitrates of the tetrasubstituted phosphonium and arsonium bases in water, when compared with the corresponding chlorides and bromides, and the extremely good solubility of ammonium nitrate and the halides, to obtain the nitrates of these tetrasubstituted bases we used the method of reacting hot concentrated solutions of ammonium nitrate and either the bromides or chlorides of the tetraarylphosphonium and tetraarylarsonium bases. The use of ammonium nitrate in amounts, exceeding by 2-2.5 times the amount theoretically required by the reaction equation, assured obtaining close to theoretical yields of the pure nitrates.

The proposed method can also be used for the preparation of other similar salts.

EXPERIMENTAL

Triphenylbenzylphosphonium Nitrate $(C_6H_5)_3(C_6H_5CH_2)PNO_3$. We synthesized triphenylbenzylphosphonium chloride (yield of pure product 81%) [7], serving as the starting product for the preparation of the nitrate, by heating triphenylphosphine, obtained by the Pfeiffer method as improved by Ya. Ya. Dodonov and G. V. Medoks [6], with benzyl chloride on the water bath.

A solution of 6 g of triphenylbenzylphosphonium chloride in 15 ml of boiling water was treated with a boiling solution of 2.6 g ammonium nitrate in 5 ml of water. The obtained heavy oily liquid soon crystallized. After one-hour heating on the water bath the reaction products were cooled to room temperature. The crude triphenylbenzylphosphonium nitrate was crushed with a spatula, filtered under reduced pressure, and washed twice with water (3 ml portions). Then it was recrystallized from 115 ml of boiling water, suction-filtered from the cooled mother liquor, the needlelike crystals washed with water (3 and 5 ml portions), and finally it was dried in a vacuum-desiccator over sulfuric acid. Yield of pure salt 5.71 g. Another 0.31 g of the same substance was isolated from the mother liquor. Total yield of nitrate 93.9%.

Tetraphenylphosphonium Nitrate $(C_6H_5)_4PNO_3$. The starting tetraphenylphosphonium bromide was obtained from phenylmagnesium bromide and phosphorus trichloride [8]. A solution of 12 g of anhydrous tetraphenylphosphonium bromide in 40 ml boiling water was treated with a hot solution of 5.7 g of ammonium nitrate in 10 ml of water. The oily liquid, collecting on the bottom of the flask, crystallized. The reaction products were allowed to stand for 24 hours. Then the solid substance was comminuted, filtered under reduced pressure, washed with cold water, and finally recrystallized from boiling water. After removing the cold mother liquor by suction-filtration the product was washed twice with cold water and then dried in a vacuum-desiccator over sulfuric acid. Yield of pure salt 11.04 g (96.1%).

Triphenylbenzylarsonium Nitrate $(C_6H_5)_3(C_6H_5CH_2)AsNO_3$.

Triphenylbenzylarsonium bromide was obtained from triphenylarsine [9] and benzyl bromide by heating on the water bath in a carbon dioxide atmosphere, precipitation of the salt with diethyl ether, and its recrystallization from boiling ethyl alcohol with the subsequent addition of diethyl ether.

A solution of the above mentioned bromide (11.5 g) in 42 ml of hot water was treated with a hot solution of 4.8 g of ammonium nitrate in 9 ml of water. The oily liquid obtained here crystallized immediately. After a day the solid product, consisting of the triphenylbenzylarsonium nitrate, was crushed, filtered under reduced pressure, washed twice with water (2 ml portions), and placed in a vacuum-desiccator; The crude substance (10.87 g) was extracted 4 times with heating, first with water (30 ml), and then with the mother liquor, remaining after the extract was cooled and the needlelike crystals of triphenylbenzylarsonium nitrate isolated from it. The crystals of the latter, after removing the mother liquor by suction-filtration and washing with 2 ml of water, were dried in a vacuum-desiccator over sulfuric acid. The yield of the pure nitrate was 10.52 g (95%).

SUMMARY

1. A method was developed for the preparation of the nitrates of tetrasubstituted phosphonium and arsonium bases from either the chlorides or bromides and ammonium nitrate without resorting to the use of silver compounds.

2. Triphenylbenzylphosphonium, tetraphenylphosphonium and triphenylbenzylarsonium nitrates were obtained in respective yields of 93.9, 96.1 and 95%.

LITERATURE CITED

[1] G. V. Medoks, and co-workers, J. Appl. Chem., 13, 1529 (1940); Sci. Memoirs Saratov State Univ., Chem. Series, 34, 121 (1954); J. Anal. Chem., 1, 319 (1946); H. Willard and G. Smith, Ind. Eng. Chem., 11, 186, 269 (1939).

[2] G. V. Medoks and N. N. Sakharova, Proc. Acad. Sci. USSR, 73, 1201 (1950).

[3] Blicke, Safir, J. Am. Chem. Soc., 63, 1493 (1941; G. V. Medoks and N. N. Sakharova, Sci. Memoirs Saratov State Univ., Chem. Series, 34, 117 (1954).

[4] Ledermann, Ber., 21, 405 (1888); G. A. Razuvaev, and co-workers, J. Gen. Chem., 5, 570, 575, 721 (1935).

[5] J. Meisenheimer, and co-workers, Lieb. Ann., 449, 213 (1926).

[6] J. Dodonov and G. Medoks, Ber. 61, 907 (1928).

[7] A. Michaelis, Soden, Lieb. Ann., 229, 295 (1885).

[8] G. Medoks, E. Soshestvenskaya and N. Sakharova, J. Appl. Chem., 25, 1113 (1952).*

[9] Pope, Turner, J. Chem. Soc., 117, 1447 (1920).

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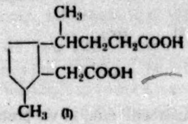
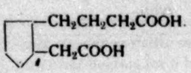
* Original Russian pagination. See C.B. translation.

SYNTHESES IN THE CYCLOPENTANONECARBOXYLIC ACID SERIES

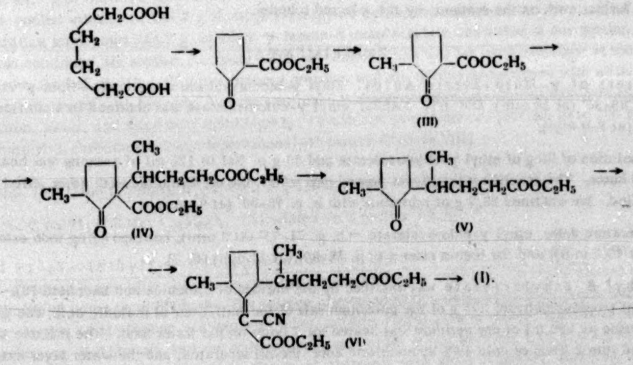
V. G. Yashunsky and V. F. Vasilyeva

[1-(3-Methyl-2-carboxymethyl)-cyclopentyl-4'-valeric acid (I), serving as the starting compound for the synthesis of some 1,4-dimethyl-7-alkylazulenes, is a very difficultly available substance [1]. It seemed of interest to attempt its synthesis from adipic acid, proceeding by the scheme proposed by F. Sorm [2] for the preparation of [1-(2-carboxymethyl)-cyclopentyl]-4'-butyric acid (II):


(I)


(II)

To obtain (I) we proposed the following series of transformations:

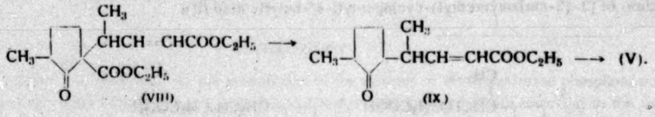

(III) (IV) (V) (VI)

Proceeding from diethyl adipate by the described method [3], we prepared ester (III) and condensed it with ethyl γ-bromovalerate. Here the yield of the keto diester was small, apparently due to the low reactivity shown by the bromo ester. In this connection we attempted to synthesize the γ-iodovalerate from

the γ-chlorovalerate by treatment of the latter with sodium iodide in alcohol and acetone solution, without however obtaining any positive results. Our experiments again confirmed the validity of the data [4] relative to the low lability of a halogen atom found at a secondary carbon atom in the γ-position to the ester group.

We were able to add a side chain to ester (III) by using the ethyl ester of γ-bromo-β-ethylacrylic acid (VII), in which the bromine atom is more labile due to the presence of the double bond in the allyl position.

The unsaturated ester (VII) was obtained by the reaction of bromosuccinimide with ethyl β-ethylacrylate in the presence of benzoyl peroxide. The condensation of esters (III) and (VII) enabled us to obtain the unsaturated keto diester (VIII) in 74.2 % yield, which by hydrogenation was converted to ester (IV), and then by saponification and esterification to ester (V).* However, the latter ester was obtained in a better yield and in purer form from (VIII) via the same steps, but in a different order, and specifically: saponification, esterification and hydrogenation:



The next step – the condensation of ester (V) with cyanoacetic ester in the presence of potassium ethylate – proceeded in very small yield, probably as the result of the sharply reduced reactivity shown by the keto group of the cyclopentanone nucleus due to the presence of substituents on both of the α-carbon atoms, one of which is secondary.

Analysis of the condensation product of cyanoacetic ester with (V) confirmed the fact that we had obtained the desired cyano diester (VI).

The unpromising results of the experiments on the reaction with cyanoacetic ester caused us to discontinue further work on the synthesis by the selected scheme.

EXPERIMENTAL

Esters of γ-Halovaleric Acids. Ethyl γ-bromovalerate was prepared from γ-valerolactone [6], b. p. 88-90° (at 10 mm) and n^{20}_D 1.4522; ethyl γ-chlorovalerate was obtained in a similar manner, b. p. 73° (at 8-9 mm).

A solution of 25 g of ethyl γ-chlorovalerate and 30 g of NaI in 125 ml of acetone was heated at the boil for 6 hours. The reaction mixture was poured into water, the oil extracted with ether, dried over $CaCl_2$, and distilled. We obtained 23,7 g of substance with b. p. 75-90° (at 9 mm).

Literature data: ethyl γ-chlorovalerate – b. p. 71-73° (at 9 mm), corresponding iodo ester – b. p. 102.5° (at 10.5 mm), and the bromo ester – b. p. 88-90° (at 11 mm) [6, 7].

Ethyl β-Ethylacrylate was obtained by the method of Canonica and Bacchetti [8]. A mixture of 160 g of propionaldehyde, 375 g of the potassium salt of the half-ester of malonic acid, 250 g of pyridine hydrochloride an 280 ml of dry pyridine was heated for 7 hours on the water bath. The mixture after cooling was poured into 2 liters of cold 10% hydrochloric acid, the oil separated, and the water layer extracted with ether. Distillation gave 163 g (57.7%, based on the potassium salt) of ethyl β-ethylacrylate with b.p. 152-158°.

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* At the time when the present study was nearly finished a communication appeared [5], in which a similar scheme for the preparation of [1-(2-carboxymethyl)-cyclopentyl]-4'-valeric acid was briefly described.

Ethyl γ-Bromo-β-ethylacrylate (VII). A mixture of 160 g of ethyl β-ethylacrylate, 225 g of freshly prepared bromosuccinimide and 1.5 g of benzoyl peroxide in 800 ml of dry carbon tetrachloride was heated at the boil for 2 hours. The succinimide obtained on cooling was filtered and washed with carbon tetrachloride. The filtrate was mixed with 400 ml of ether, washed with water (twice with 50 ml portions), and dried over fused magnesium sulfate. The residue obtained after distilling off the solvent was distilled under reduced pressure, and here two fractions were collected:

1st fraction, 7.5 g, b. p. 64-68° (at 28 mm), being unreacted ester; 2nd fraction, 190 g (73.4%), b. p. 86-92° (at 4 mm), being the γ-bromo-β-ethylacrylate.

Found %: C 40.76; H 5.47; Br 38.76. $C_7H_{11}O_2Br$. Calculated %: C 40.56; H 5.35; Br 38.56.

Ethyl 3-Methyl-2-cyclopentanone-1-carboxylate (III) [3]. Diethyl-α-methyladipate (57.4 g), obtained by the methylation and subsequent cleavage of ethyl 2-cyclopentanone-1-carboxylate, was gradually added with stirring to a suspension of 6.5 g of metallic sodium in 170 ml of boiling toluene. The congealed reaction mass was heated for another hour at 130-140°, and the next day was decomposed with dilute acetic acid. The toluene layer was separated, the water layer extracted with toluene, and the combined toluene solution dried over fused magnesium sulfate. The oil remaining after distilling off the solvent was distilled under reduced pressure. We obtained 33.4 g (74%) of ethyl 3-methyl-2-cyclopentanone-1-carboxylate with b. p. 109° (12 mm). Literature: b. p. 108-109° (13 mm).

Condensation of the Ethyl Esters of γ-Bromovaleric and 3-Methyl-2-cyclopentanone-1-carboxylic Acids. To 1.17 g of finely divided metallic sodium in 30 ml of boiling toluene with stirring and heating was added 8.5 g of (III), then after heating for 3 hours 7 g of the γ-bromovalerate was added at one time, and the reaction mixture was heated for another 14 hours at 130-140°. After decomposing with water the aqueous layer was extracted with ether. The combined ether-toluene solution was washed with water, dried over magnesium sulfate, and distilled. The 1st fraction, 14.4 g, b. p. 90-130° (at 1 mm), was a mixture of the starting esters; the 2nd fraction, 0.32 g, b. p. 130-131° (at 1 mm), was apparently the condensation product.

Condensation of the Ethyl Esters of 3-Methyl-2-cyclopentanone-1-carboxylic and γ-Bromo-β-ethylacrylic Acids. To a solution of sodium alcoholate cooled to -17°, prepared from 24.7 g of metallic sodium and 470 ml of anhydrous ethyl alcohol, was added in two portions with stirring a cooled solution of 182.2 g of ethyl 3-methyl-2-cyclopentanone-1-carboxylate. After stirring at this temperature for 2 hours 244.2 g of ethyl γ-bromo-β-ethylacrylate was added in one portion, and the stirring was continued for another 3.5 hours. The reaction mixture was let stand overnight at room temperature, the alcohol distilled off under reduced pressure, and the residue decomposed with water. The water layer was extracted with benzene, and the combined benzene solution was washed with 10% H_2SO_4, $NaHCO_3$ solution, water, and dried over fused $MgSO_4$. Distillation under reduced pressure gave 235 g of ethyl [1-(3-methyl-1-carbethoxy)-2-cyclopentanone]-4'-penten-2'-oate(VIII).

B. p. 150-154° (and 0.5 mm), n_D^{20} 1.4732, d_4^{20} 1.0800, MR_D 77.00; calc. 76.74.

Found %: C 65.04; H 8.05. $C_{16}H_{24}O_5$. Calculated %: C 64.84; H 8.16.

Ethyl [1-(3-Methyl)-2-cyclopentanone]-4'-penten-2'-oate (IX). 220 g of the above-obtained ester (VIII), 360 ml of concentrated hydrochloric acid and 360 ml of glacial acetic acid was boiled for 8 hours in an oil bath. The residue after evaporation under reduced pressure was treated with $NaHCO_3$ solution until alkaline, washed with ether, acidified until acid to Congo, and extracted with ether. The ether was distilled off, and the residue was heated under reflux with one liter of a 3% hydrogen chloride solution in anhydrous ethyl alcohol. The usual treatment gave 105.7 g (63.5%, based on VIII) of ethyl [1-(3)methyl)-2-cyclopentanone]-4'-penten-2'-oate with b. p. 123-128° (at 0.7 mm).

Found %: C 69.54; H 8.90. $C_{13}H_{20}O_3$. Calculated %: C 69.62; H 8.99.

Ethyl [1-(3-Methyl-1-carbethoxy)-2-cyclopentanone]-4'-valerate (IV). A solution of 54 g of the unsaturated keto diester (VIII) in 100 ml of ethyl alcohol was hydrogenated at room temperature and atmospheric pressure with 5 g of 10% Pd/$CaCO_3$. After 24 hours the hydrogen absorption was 3905 ml (calculated for theory 4700 ml H_2). Distillation gave 41.4 g (76%) of ethyl [1-(3-methyl-1-carbethoxy)-2-cyclopentanone]-4'- valerate with b.p. 145-150° (at 0.35 mm).

Ethyl [1-(3-Methyl)-2-cyclopentanone]-4'-valerate (V)

A. Ethyl [1-(3-methyl)-2-cyclopentanone]-4'-penten-2'-oate (IX) was hydrogenated in ethyl alcohol with 10% Pd/$CaCO_3$ in the same manner as before. The ethyl [1-(3-methyl)-2-cyclopentanone]-4'-valerate was obtained in 73% yield; b. p. 122.5-124.5° (at 0.5 mm).

Semicarbazone, m. p. 151-152° (from 40% ethyl alcohol).

Found %: C 58.88; H 8.93. $C_{14}H_{25}O_3N_3$. Calculated %: C 59.33; H 8.89.

B. Ester (IV) (43.4 g) was saponified with a mixture of hydrochloric and acetic acids (8 hours) and the acid, without being distilled, was esterified with a 3% alcoholic solution of hydrogen chloride. Two distillations gave 16.9 g of substance with b. p. 128-140° (at 0.4 mm).

Condensation of Ethyl [1-(3-Methyl)-2-cyclopentanone]-4'-valerate With Cyanoacetic Ester. A mixture of 26.15 g of ethyl [1-(3-methyl)-2-cyclopentanone]-4'-valerate (obtained by method A) and the potassium derivative of cyanoacetic ester, prepared from 23.1 g of cyanoacetic ester, 7.95 g of potassium and 100 ml of anhydrous ethyl alcohol, was let stand for 12 days at room temperature. Then the reaction mixture was poured into cooled dilute sulfuric acid, extracted with ether, the ether extract washed with soda solution, then with water, and dried over fused $MgSO_4$. Fractional distillation gave 3.47 g of substance with b. p. 169-175° (at 0.5 mm); redistillation of this fraction gave an oil (1.78 g) with b. p. 175-178° (at 0.7 mm).

Found %: C 66.86; H 8.40; N 4.62. $C_{18}H_{27}O_4N$. Calculated %: C 67.26; H8.47; N 4.36.

SUMMARY

Ethyl [1-(3-methyl)-2-cyclopentanone]-4'-valerate was obtained via a number of steps. Its condensation with cyanoacetic ester proceeds in small yield, apparently due to the reduced reactivity shown by the keto group.

LITERATURE CITED

[1] F. Sorm, J. Gut, J. Hlavnicka, J. Kucera, L. Sedivy, Coll. Czech. Chem. Comm., 16, 168 (1951).

[2] F. Sorm, Coll. Czech. Chem. Comm. 12, 251 (1947).

[3] W. Dieckmann, Lieb. Ann., 317, 73 (1901).

[4] J. W. Cook, C. A. Lawrence, J. Chem. Soc., 823, 1937.

[5] W. Herz, J. Am. Chem. Soc., 76, 3349 (1954).

[6] H. Staudinger, L. Ruzicka, Helv. Chim. Acta, 7, 249 (1924).

[7] H. Wohlgemuth, C. r., 158, 1578 (1914).

[8] L. Canonica, T. Bacchetti, Gazz., 83, 1043 (1953); Abst. J. Chem., 1954, 47,982.

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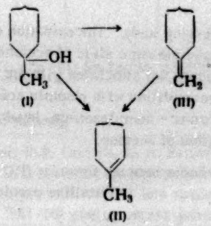
S. Ordzhonikidze All-Union
Scientific-Research Chemical-Pharmaceutical Institute

STUDY OF THE STRUCTURE OF THE TRITERPENE ALCOHOL ZEORIN

A. A. Ryabinin and L. G. Matyukhina

Zeorin, a substance synthesized by many lichens, was discovered in 1876 [1]. By means of a number of investigations [2-4] it was established that zeorin is a saturated alcohol with the composition $C_{30}H_{52}O_2$, belonging to the group of pentacyclic triterpenes. The zeorin molecule contains two hydroxyl groups: a secondary OH that is found in the six-membered ring, and a tertiary OH that, according to Barton and Bruun [4], is found in one of the rings at the carbon atom attached to the methyl group.



This postulation was based on the formation of two isomers in the dehydration of zeorin (I)—zeorinin (II) and isozeorinin (III). A study of the spectra of these substances revealed that (II) has either a tri- or tetrasubstituted double bond, while (III) has a vinylidene group. Isozeorinin is converted to zeorinin under the influence of acids.

The complexity of establishing the structure of zeorin is associated with the absence in its molecule of a hydroxyl group on the second carbon atom and of a double bond, both of which are usually found in triterpene compounds of a similar nature. This circumstance prevents its conversion into one of the numerous substances of the given group with a known structure. The saturated hydrocarbon, obtained from zeorin, proved to be new.

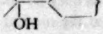
In our investigation we attempted to expand the existing information on the structure of zeorin by making a study of the products of its destructive oxidation. We obtained zeorin from a new source, and some of the differences in its properties when compared with those described in the literature made necessary its complicated identification by the method of preparing a number of derivatives. A comparison of the constants given in Table 1 reveals that this identification was achieved.

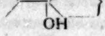
The oxidation of zeorin with chromic acid at room temperature or at 40-60° resulted in the cleavage of acetone, the amount of which was as high as 0.68 mole. The other decomposition product, isolated in 0.3 mole amount, proved to be the previously unknown acid $C_{27}H_{42}O_4$ with m. p. 244-246° (cor.), $[\alpha]_D$ - 3.8°.

This acid has one active keto group and forms the monosemicarbazone with m. p. 226° (decompn., cor.). Its methyl ester melts at 147-148°, $[\alpha]_D$ - 1.1°; it does not contain an active hydrogen, as determined by the Tserevitinov method. The infrared spectrum of this substance shows absorption maxima at 1706 and 1730 cm^{-1}. The first of them is associated with the presence of a keto group in the six-membered ring, and the second characterizes a keto group, located either in the five-membered ring or the ester group.

The conditions used to obtain the acid and the absence in its molecule of a tertiary hydroxyl determine the function of the second oxygen atom as being an inactive keto group. Such a keto group, not entering into the usual reactions, is formed in the oxidation of the secondary hydroxyl group found in zeorin, which was shown by Barton and Brunn, and confirmed by us.

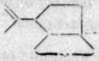
As a result, the oxidation of zeorin leads to the cleavage of acetone, the disappearance of the tertiary hydroxyl group, and the formation of an active keto group. All of this leads to the postulation that zeorin contains an isopropyl group, to which the tertiary hydroxyl group is attached (either IV or V). Consequently, one of the rings in zeorin should be five-membered.

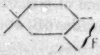

(IV)


(V)

This postulation was supported by the following study. The oxidation of zeorin monoacetate, in which the secondary hydroxyl group is acylated [4], gave the same yield of acetone as was obtained from zeorin. Consequently, the cleavage of the isopropyl group is not associated with the oxidation of that portion of the molecule containg the secondary hydroxyl. The oxidation with chromic acid or permanganate and the ozonolysis of the dehydration product of this acetate – acetylzeorinin, in which the tertiary hydroxyl group had been eliminated, did not lead to the formation of acetone.

Further observations made it possible to choose between formulas (IV) and (V). The ozonolysis of zeorinin acetate gave us 0.04 mole of formaldehyde and a crystalline ozonide $C_{32}H_{52}O_5$ with m. p. 196-197° (decompn., cor.) was isolated; on prolonged heating the m. p. was 191-196° (decompn. cor.). This ozonide is not decomposed when boiled with water, whereas under the same conditions the ozonides formed from isopropylidene and vinylidene groups cleave either acetone or formaldehyde, respectively. Stable ozonides are characteristic for the double bonds of condensed hydroaromatic rings. The formation of an endocyclic double bond in the dehydration of zeorin supports structure (V). However, this is refuted by the formation of formaldehyde in the ozonolysis, indicating the presence of a small amount of zeorinin isomer with a vinylidene group. The formation of this isomer (isozeorinin), as indicated above, was also observed by Barton and Bruun. The contradiction will be eliminated if it is assumed that zeorin has the partial formula (IV), and that its transformation into zeorinin is associated with dehydration and rearrangement. Such a rearrangement proceeds very easily under the influence of mineral and formic acids in the lupeol group (VI) and leads to an expansion of the ring at the expense of the isopropenyl group and the creation of an endocyclic double bond (VII) [5]. The formation of zeorinin and the transformation of isozeorinin into zeorinin proceed under completely similar conditions.


(VI)



(VII)

		Literature data		Our data
		[2, 3]	[4]	
Zeorin $C_{30}H_{52}O_2$	Melting point	253°	223—227°	223.5—227.5° (cor.)
	$[\alpha]_D$*	+101.4° (pyridine)	+54°	+56° ($c = 1.26$) +67° ($c = 0.69$)(pyridine)
Zeorin acetate $C_{32}H_{54}O_3$	Melting point	225—227°	225—230°	220—223° (cor.)
	$[\alpha]_D$	—	+78°	+78° ($c = 3.08$)
Zeorinin $C_{30}H_{50}O$	Melting point	181—183°	179—183°	177—184° (cor.)
	$[\alpha]_D$	+50.00°	+59°	+55° ($c = 0.94$)
Zeorinin acetate $C_{32}H_{52}O_2$	Melting point	197—200°	200—205°	191.5—196° (cor.)
	$[\alpha]_D$	—	+70°	+69° ($c = 2.19$)
Zeorinone $C_{30}H_{50}O_2$	Melting point	—	239—245°	251—254° (cor.)
Zeorininone $C_{30}H_{48}O$	Melting point	184°	177—178°	173—177° (cor.)
Desoxyzeorin acetate $C_{32}H_{54}O_2$	Melting point	182—183°	202—203°	189—192° (cor.)
	$[\alpha]_D$	—	+51°	+41° ($c = 0.24$)

The partial formulas (IV), (VII) and (VI) for zeorin, zeorinin and isozeorinin agree with all of the known experimental facts.

Our study of zeorin is being continued.

We are deeply indebted to Prof. V. P. Savitch, K. A. Rassadina and E. N. Moiseeva for the botanical determinations and for supplying us with material for our studies.

EXPERIMENTAL

1. Isolation and Identification of Zeorin. The ground lichens Cladonia deformis Hoffm. were extracted with boiling chloroform. The crystalline precipitate obtained from the evaporation of this solution was freed from usninic acid by treatment with aqueous alkali and repeated recrystallization from dioxane. The yield of zeorin was 0.25%.

Zeorin acetate, zeorinin and its acetate, zeorininone, zeorinone and desoxyzeorin acetate were obtained by the methods used by Barton and Bruun. The properties of all of these substance are given in Table 1. The analyses agreed with the given molecular formulas.

2. Acid $C_{27}H_{42}O_4$. A slurried suspension of 13.3 g of zeorin in 325 ml of glacial acetic acid was slowly treated with concentrated chromic acid, prepared from 12 g of chromic anhydride. After the oxidation had slackened, the remainder of the chromic acid was added and the reaction continued at 55°. After diluting with water, several milliliters of hydrochloric acid was added, and the product extracted with ether. The ether extract was washed with water, and the acids were put into solution with potash and then precipitated with hydrochloric acid. The dried mixture of acids was dissolved in the minimum amount of 10% potassium hydroxide solution and methanol, filtered, acidified with an alcohol solution of hydrogen chloride, and the obtained acid separated.

The neutral fraction of substances, remaining in the ether, was again oxidized with 4 g of chromic anhydride under the same conditions as before; here some more of the acid was obtained. The total yield of acid was 3.9 g. After recrystallization from dioxane, m. p. 244–246°, $[\alpha]_D$ − 3.8° (c = 1.41).

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* If the solvent is not indicated, all of the $[\alpha]_D$ values given in this paper were determined in chloroform solutions.

Found %: C 75.23, 75.25, 75.32, 75.36; H 9.70, 9.71, 9.73, 9.89. $C_{27}H_{42}O_4$. Calculated %: C 75.30; H 9.83.

After separating the precipitate of acid $C_{27}H_{42}O_4$ the acid alcohol solution was diluted with water; here a substantial amount of amorphous acids separated, the separation of which we were unable to effect.

The methyl ester of the acid was obtained by treatment with diazomethane in ether solution, and also by boiling a solution of the acid in a mixture of methanol and sulfuric acid. After recrystallization from methanol it melted at 147-148° (cor.), $[\alpha]_D$ − 1.1° (c = 0.71).

Found %: C 75.49, 75.53, 75.40; H 9.85, 9.99, 9.79. $C_{28}H_{44}O_4$. Calculated %: C 75.63; H 9.97

Analysis of the silver salt of the acid. Found %: C 60.30, 60.27; H 7.79, 7.72; Ag 19.98, 19.84. $C_{27}H_{41}O_4Ag$. Calculated %: C 60.33; H 7.69; Ag 20.07.

The monosemicarbazone was obtained after 10-day standing of a solution of the acid and semicarbazide hydrochloride in pyridine.

Found %: N 8.73. $C_{28}H_{45}N_3O_4$. Calculated %: N 8.62.

3. The Oxidation of Zeorin and Its Derivatives With Chromic Acid was achieved by either dissolving or suspending them in acetic acid. The acetone was steam-distilled and identified either as the p-nitrophenylhydrazone or as the 2,4-dinitrophenylhydrazone (Table 2).

TABLE 2

Substance	Amount (in g)		Oxidation temperature	Yield of acetone (in moles from 1 mole of substance)
	Substance	Chromic anhydride		
Zeorin.	4.44	3.0	42–44°	0.68
Zeorin.	0.50	0.25	20	0.23
Zeorin acetate.	4.10	1.7	65–66	0.54
Zeorinin acetate.	0.45	0.2	53	0

The oxidation of zeorinin and of its acetate with potassium permanganate in acetic acid led to the formation of neither acetone nor formaldehyde.

4. Zeorinin Acetate Ozonide. 1) A mixture of 0.67 g of the acetate and 30 ml of glacial acetic acid was treated with a stream of 6% ozone at 20° for 2 hours. Then the mixture was diluted with water and boiled for an hour. The volatile substances were steam-distilled. The presence of acetone in the condensate could not be shown. Formaldehyde was isolated as the dimedone compound (0.011 g), which was identified by the mixed melting point test. After removal of the volatile substances by distillation the remaining ozonolysis products were extracted with ether. Recrystallization from an alcohol-benzene mixture gave 0.16 g of the ozonide.

2) Zeorinin acetate, dissolved in carbon tetrachloride, was ozonized under the same conditions as before. The solvent was vacuum-distilled at room temperature. The crystalline precipitate, washed with a small amount of ether, proved to be identical with the ozonide obtained earlier. The melting point of this substance was 196-197° (decompn., cor.); on prolonged heating it melted at 191-196°. The ozonide colors sulfuric acid a bright yellow.

Found %: C74.22, 74.22, 74.46; H 10.05, 10.15, 10.15. $C_{32}H_{52}O_5$. Calculated %: C 74.37; H 10.14.

SUMMARY

The destructive oxidation of the triterpene alcohol zeorin was studied. The presence of an isopropyl group was established connected to a pentacyclic system, and also the probable position of the tertiary hydroxyl group. A new interpretation was proposed for the transformations of zeorin into zeorinin and isozeorinin, and also of isozeorinin into zeorinin.

LITERATURE CITED

[1] Elsevier's Encyclopaedia of Org. Chem., series III, v. 14, Suppl. (1952).

[2] Y. Asahina, H. Akagi, Ber., 71, 980 (1938).

[3] Y. Asahina, I. Yosioka, Ber., 73, 742 (1940).

[4] D. H. R. Barton, T. Bruun, J. Chem. Soc., 1952, 1683.

[5] T. R. Ames, J. L. Beton, A. Bowers, T. G. Halsall, E. R. H. Jones, J. Chem. Soc., 1954, 1905.

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Botanical Institute
Academy of Sciences of the USSR

SUMMARY

The derivative [illegible] of [illegible] was [illegible]. The presence of [illegible] group was established [illegible] and [illegible] position of the [illegible] hydroxyl group. A new [illegible] was proposed for the [illegible] and [illegible], and also of [illegible].

LITERATURE CITED

[1] Elsevier's Encyclopaedia of Org. Chem., series III, v. [illegible], Suppl. (195[illegible]).

[2] Y. Asahina, [illegible] 73, 982 (195[illegible]).

[3] Y. Asahina, I. Yosioka, Ber., [illegible] (19[illegible]).

[4] D. H. R. Barton, T. Bruun, J. Chem. Soc., 195[illegible].

[5] T. R. Ames, J. L. Beton, A. Bowers, T. G. Halsall, E. R. H. Jones, J. Chem. Soc., 1954, [illegible].

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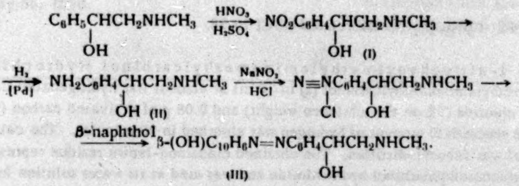
SOME REACTIONS OF HALOSTACHINE

G. M. Borodina

As a supplement to a previous communication, published earlier [1], we describe here some of the synthesis reactions of halostachine (phenylmethylaminomethylcarbinol). The reactions, run with both of the optical isomers of halostachine, were the following:



$$C_6H_5\underset{OH}{\underset{|}{C}}HCH_2NHCH_3 \xrightarrow[H_2SO_4]{HNO_3} NO_2C_6H_4\underset{OH}{\underset{|}{C}}HCH_2NHCH_3 \ \text{(I)} \longrightarrow$$

$$\xrightarrow[\text{[Pd]}]{H_2} NH_2C_6H_4\underset{OH}{\underset{|}{C}}HCH_2NHCH_3 \ \text{(II)} \xrightarrow[HCl]{NaNO_2} N{\equiv}\underset{Cl}{\underset{|}{N}}C_6H_4\underset{OH}{\underset{|}{C}}HCH_2NHCH_3 \longrightarrow$$

$$\xrightarrow{\beta\text{-naphthol}} \beta\text{-(OH)}C_{10}H_6N{=}NC_6H_4\underset{OH}{\underset{|}{C}}HCH_2NHCH_3. \ \text{(III)}$$

The nitration reaction was run by the modified method described for the nitration of racemic phenylalkylaminomethylcarbinols [2]. The *l*- and d-nitrophenylmethylaminomethylcarbinols were isolated as the hydrochlorides and were reduced in the presence of palladium-on-carbon to the corresponding *l*- and d-aminophenylmethylaminoethylcarbinols (II). In view of their instability the hydrochlorides of the *l*- and d-aminophenylmethylaminomethylcarbinols were diazotized without their previous isolation. The obtained diazo compounds were coupled with β-naphthol by the Fierz-David method [3].

The position of the nitro group in the ring with respect to the carbon chain of the *l*- and d- nitrophenylmethylaminomethylcarbinols, the same as the position of the diazo-component with respect to the β-naphthol, was not determined by us.

However, the data in the literature [2-4] indicate that in nitration of phenylalkylaminoalkylcarbinols the nitro group goes predominantly in the para-position, since the solitary or chief oxidation product of the obtained nitro derivatives is p-nitrobenzoic acid. In some cases the m-isomer was also isolated in the nitration.

The hydrochlorides of the l- and d-nitrophenylmethylaminomethyl carbinols (I) obtained by us has a sharp melting point (210-215° for both antipodes), which indicates the absence of the mixed para-and meta-isomers in them.

When the hydrochloride of *l*-nitrophenylmethylaminomethylcarbinol was chromatographed on No. 1 filter paper, using a butanol-water-acetic acid mixture (50:50:1) as the solvent for the upper layer, it was revealed that only one well-defined stain ($R_f = 0.16$) is present, which testifies to the purity of the described substance. This permits us to postulate that in the nitration of *l*- and d-phenylmethylaminomethylcarbinols the nitro group enters chiefly in one position, and in this connection most probably in the para-position.

As regards the coupling product with β-naphthol, it is known that in this reaction the hydroxyl group of β-naphthol is always found in the ortho-position with respect to the diazo-component.

I am deeply indebted to G. P. Menshikov for the attention devoted to the present study.

EXPERIMENTAL

Nitration of l-phenylmethylaminomethylcarbinol. To a mixture of the acids (6 parts of H_2SO_4 (d 1.84) and 6 parts of HNO_3, (d 1.36) for 1 part of base), cooled to - 2 to 0°, was slowly added 2.4 parts of the base; the reaction mixture was let stand at -2 to 0° for 4-5 hours, after which it was poured into 300-350 g of ice and cautiously neutralized with 30% potassium hydroxide solution with external cooling. The base that separated here was extracted with ether, the ether solution dried over potash, and the ether distilled off. The residual light-yellow oil was treated with an alcohol solution of hydrogen chloride until acid to Congo. The precipitate of the l-nitrophenylmethylaminomethylcarbinol hydrochloride was separated and washed with acetone. Recrystallization from alcohol gave the substance as colorless crystals, m. p. 214-215°, weight 0.9 g, $[\alpha]_D$ -44.09° (c = 7.28, water).

Found %: Cl 15.29. $C_9H_{13}O_3N_2Cl$. Calculated %: Cl 15.26.

The Nitration of d-phenylmethylaminomethylcarbinol was run by the method described for the levo isomer. From 2.7 g of substance we obtained 0.95 g of d-nitrophenylmethylaminomethylcarbinol hydrochloride with m. p. 213 – 214°, $[\alpha]_D$ + 43.81° (c = 8.24, water).

Found %: Cl 15.44. $C_9H_{13}O_3N_2Cl$. Calculated %: Cl 15.26.

Reduction of l-nitrophenylmethylaminomethylcarbinol Hydrochloride. One gram of l-nitrophenylmethylaminomethylcarbinol (I) in 30 ml of alcohol was hydrogenated in the presence of 0.02 g of palladium chloride (2% on the substance weight) and 0.05 g of activated carbon (5% on the substance weight). The theoretical amount of hydrogen was absorbed in 30 minutes. The catalyst was filtered, and the alcohol was vacuum-distilled. The obtained cinnamon-brown residue represented impure l-aminophenylmethylaminomethylcarbinol hydrochloride and was used as its water solution for the diazotization reaction.

Reduction of d-Nitrophenylmethylaminomethylcarbinol Hydrochloride was run by the method described for the levo isomer.

Diazotization of *l*-Aminophenylmethylaminomethylcarbinol Hydrochloride and Coupling of *l*-Diazophenylmethylaminomethylcarbinol With β-Naphthol. A solution of 0.95 g of *l*-aminophenylmethylaminomethylcarbinol in 12 ml of water and 10 ml of 10% hydrochloric acid was diazotized with the calculated amount of sodium nitrite. (0.32-0.33 g). A solution of 0.68 g of β-naphthol and 1.2 g of sodium carbonate in 10-15 ml of water (with the addition of 1-2 ml of 30% NaOH) was cooled to 0° for coupling. To the cold alkaline solution of β-naphthol with stirring was gradually added the soda-neutralized solution of l-diazophenylmethylaminomethylcarbinol. A red amphorous precipitate of dye (III) deposited immediately. The reaction mixture was let stand for an hour at 0-5°, and then 1 hour at 30°. The red precipitate was filtered, and then dissolved in 0.1N hydrochloric acid solution. The excess β-naphthol was extracted three times from the acid solution with ether, and the azo dye was again precipitated with 0.1N sodium hydroxide solution. After standing for 1 hour the precipitate was filtered, washed with water, and dried in a vacuum-desiccator. Weight 1.28 g. The substance is an amorphous red powder.

Found %: N 12.77. $C_{19}H_{19}O_2N_3$. Calculated %: N 13.06.

Diazotization of d-Aminophenylmethylaminomethylcarbinol Hydrochloride and Subsequent Coupling of d-Diazophenylmethylaminomethylcarbinol With β-Naphthol was run by the method described for the levo isomer. From 1 g of d-aminophenylmethylaminomethylcarbinol hydrochloride we obtained 1.37 g of azo dye (III).

Found %: N 12.67. $C_{19}H_{19}O_2N_3$. Calculated %: N 13.06.

SUMMARY

1. The nitration of *l*- and d-phenylmethylaminomethylcarbinols gave the l- and d-nitrophenylmethylaminomethylcarbinols, which were isolated as the hydrochlorides.

2. The catalytic hydrogenation of the *l*-and d-nitrophenylmethylaminomethylcarbinols in the presence of palladium-on carbon gave the *l*- and d-aminophenylmethylaminomethylcarbinol hydrochlorides, which were diazotized, and the *l*- and d-diazophenylmethylaminomethylcarbinols were coupled with β-naphthol to yield the corresponding azo dyes.

LITERATURE CITED

[1] G. P. Menshikov and G. M. Borodina, J. Gen. Chem., 17, 1569 (1947).

[2] German Patent 511, 469; Friedlander, 17, 2506; German Patent 521,729; Friedlander, 17, 2509.

[3] Fierz-David, Manufacture of Organic Dyes, p. 120 (1933).

[4] J. Barbiere, Bull. Soc. Chim., 11, 470 (1944).

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S. Ordzhonikidze All-Union
Scientific-Research Chemical-Pharmaceutical Institute